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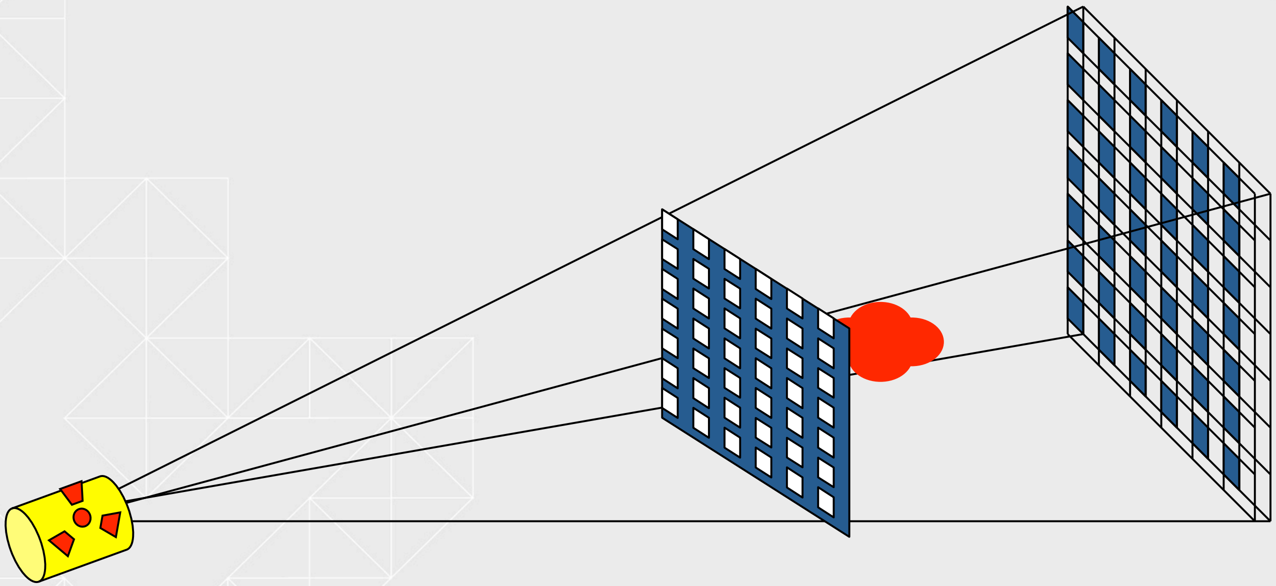
Sviluppo delle tecnologie a contrasto di fase per applicazioni mediche e biologiche - dai sincrotroni alle sorgenti X convenzionali



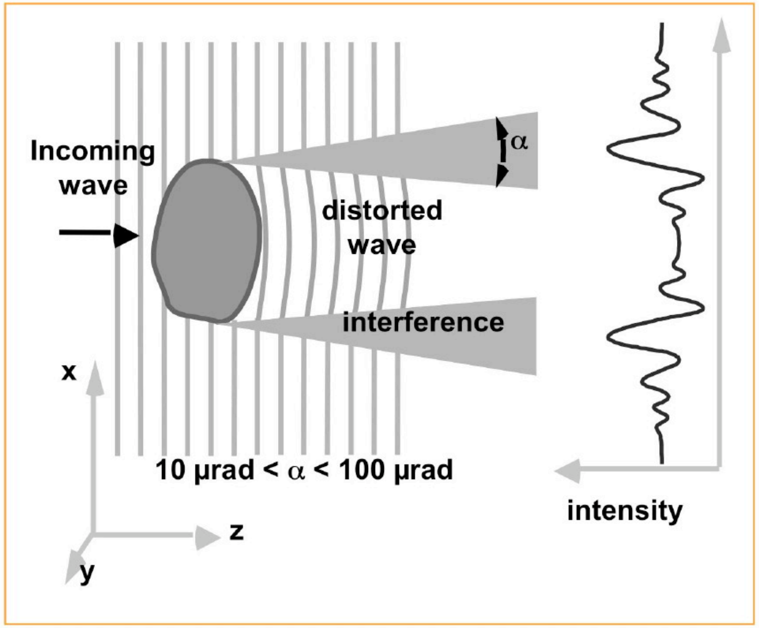
Sandro Olivo

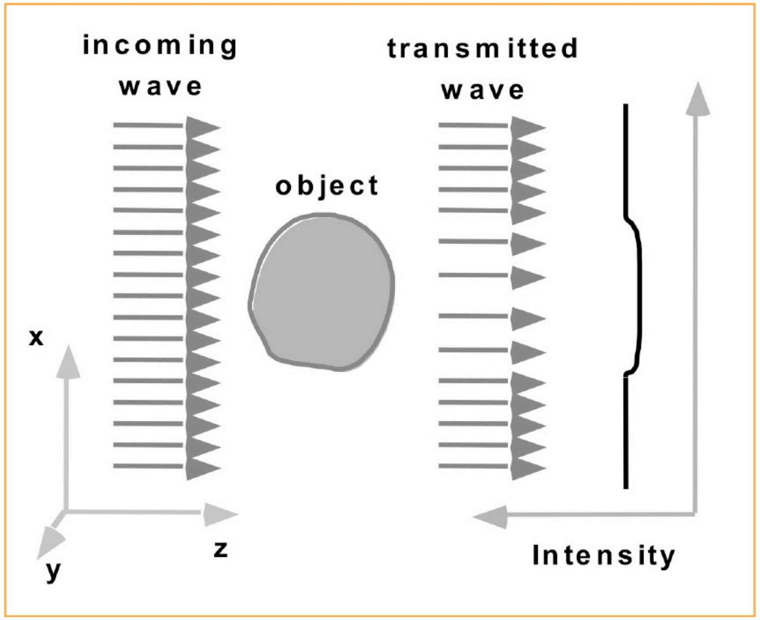
Medical Physics and Bioengineering, UCL

UCL Institute of Biomedical Engineering

Research Complex at Harwell

Phase Contrast Imaging vs. Conventional Radiology





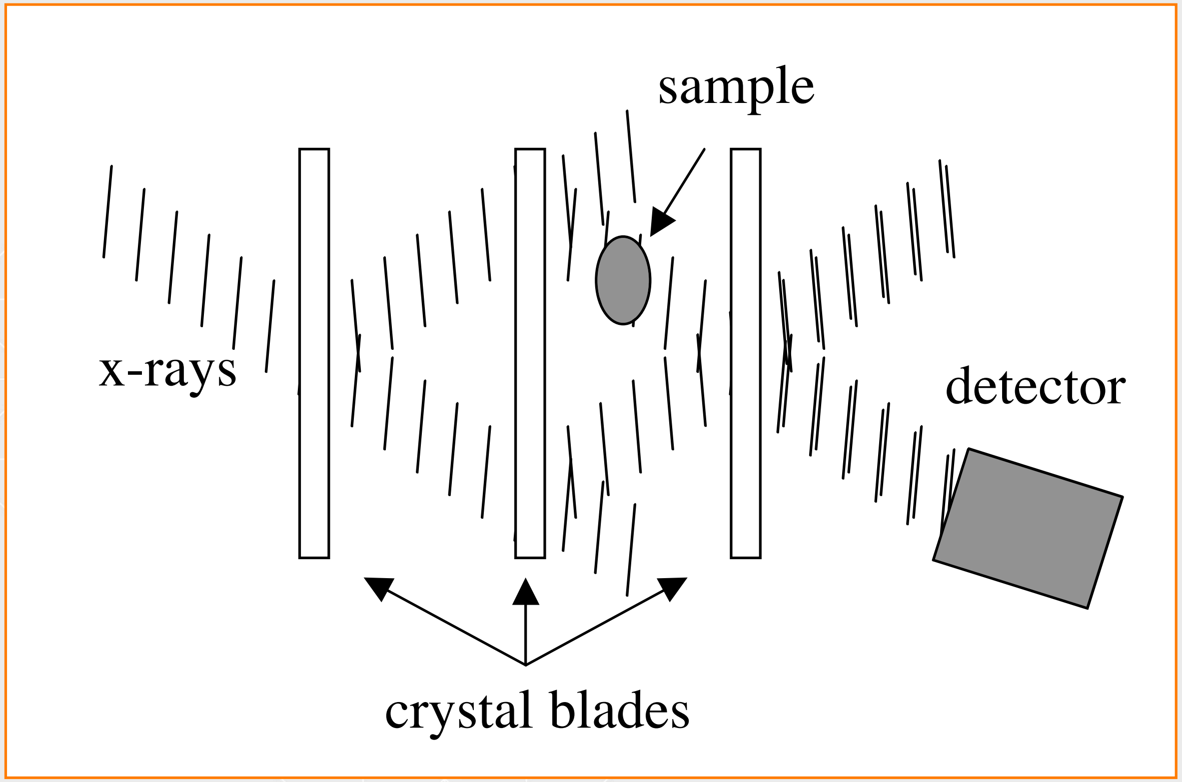
Refractive index: $n = 1 - \delta + i\beta$; $\delta >> \beta$ ->

phase contrast (**$\Delta I/I_0 \sim 4\pi\delta\Delta z/\lambda$**) >> absorption contrast (**$\Delta I/I_0 \sim 4\pi\beta\Delta z/\lambda$**)

Two possible approaches:
- **detect interference patterns**
- **detect angular deviations**

In the beginning:

The BONSE/HART interferometer (seminal 1965 APL paper)



- allows complete phase reconstruction - but:
- small fields of view
- high sensitivity to vibrations
- beam strictly parallel & monochromatic

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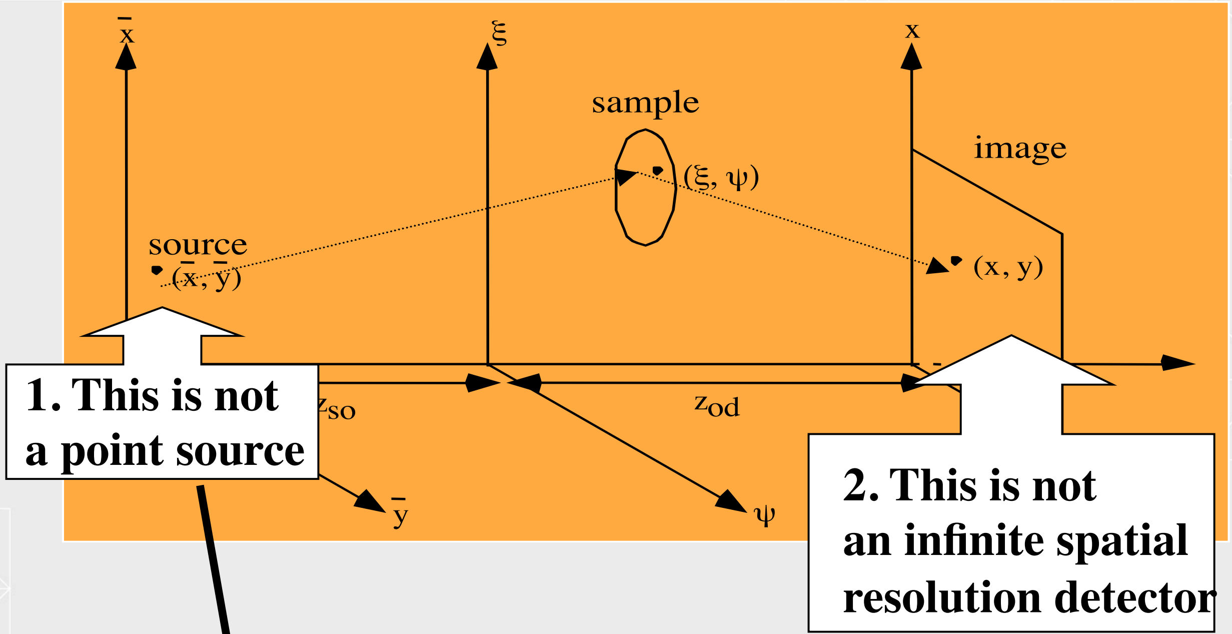
But then Momose *et al*, Med Phys 22 (1995) 375-9, Nature Medicine 2 (1996) 473-5 -> beginnings of XPCI

How can we model it?

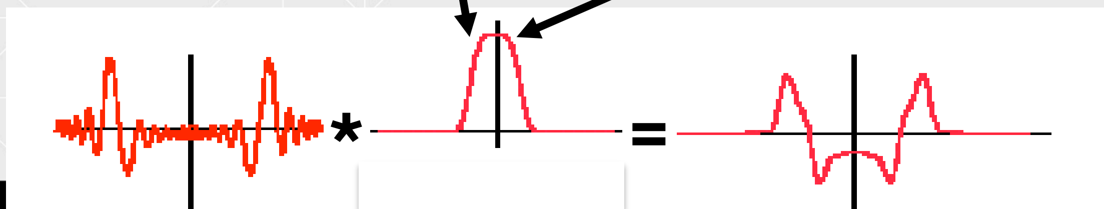


without the object:

$$E(x,y)=\frac{1}{r}\exp(i2\pi r/\lambda)$$

with the object in, it is effectively described by the Fresnel/Kirchoff integral

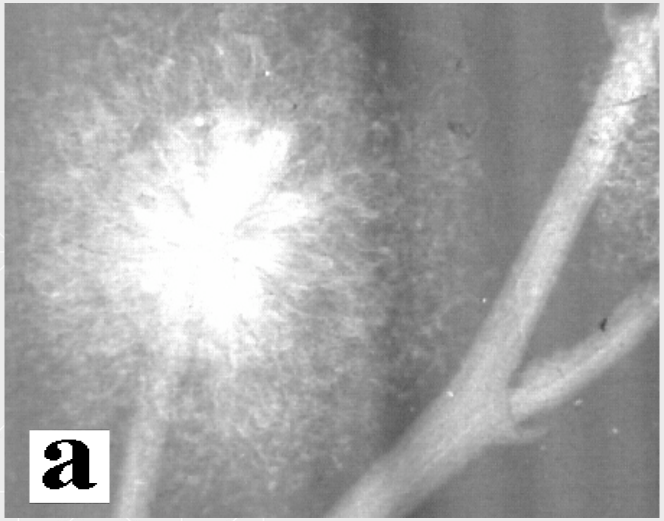
$$E(x,y)=\frac{1}{\sqrt{i\lambda z_{so}z_{od}(z_{so}+z_{od})}}\exp\{\frac{2\pi i}{\lambda}[z_{so}+z_{od}+\frac{(y-\bar{y})^2}{2(z_{so}+z_{od})}]\cdot\int_{-\infty}^{+\infty}d\xi\exp\{\frac{\pi i}{\lambda}[\frac{(\bar{x}-\xi)^2}{z_{so}}+\frac{(\xi-x)^2}{z_{od}}]\}\exp[i\Phi(\xi)]$$

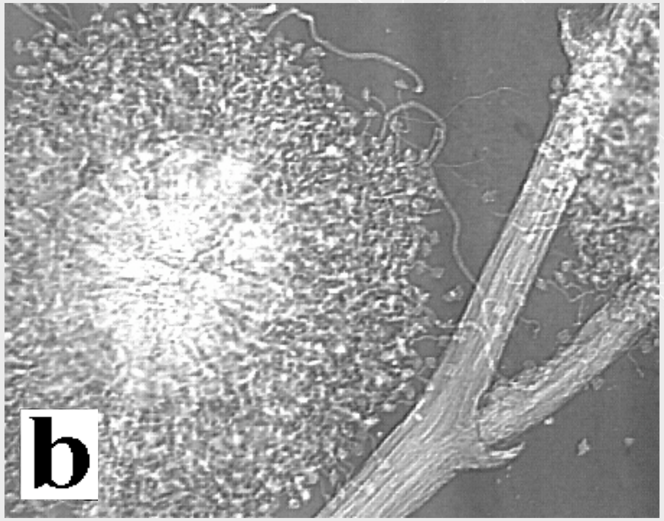


A. Olivo NIM A 548 (2005) 194-9

a) absorption

b) phase contrast



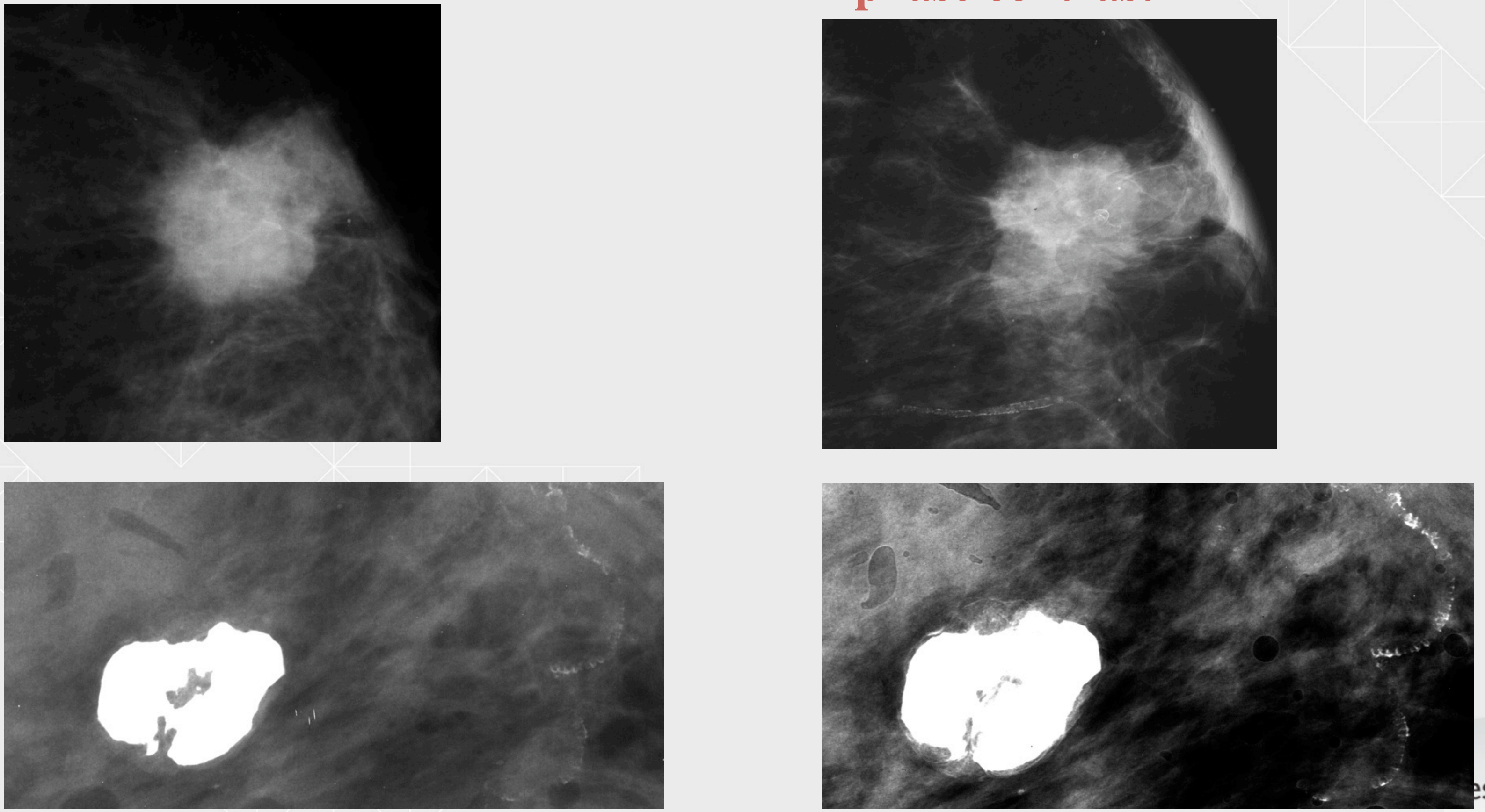


DiMichiel *et al* Proceedings of MASR1997

Impressive results are achieved in breast imaging

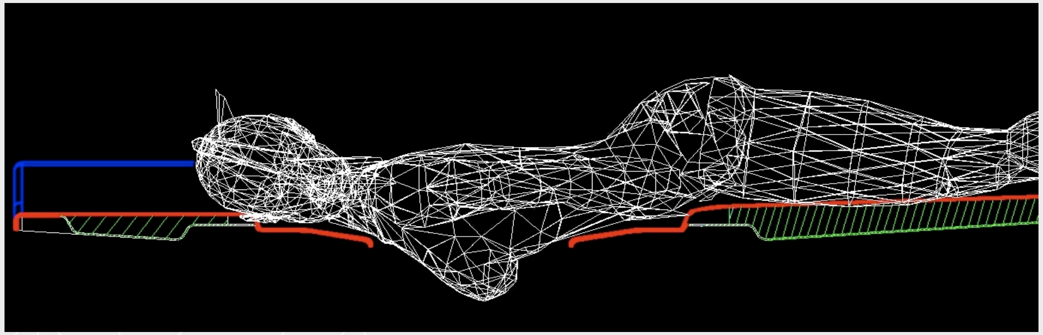
absorption

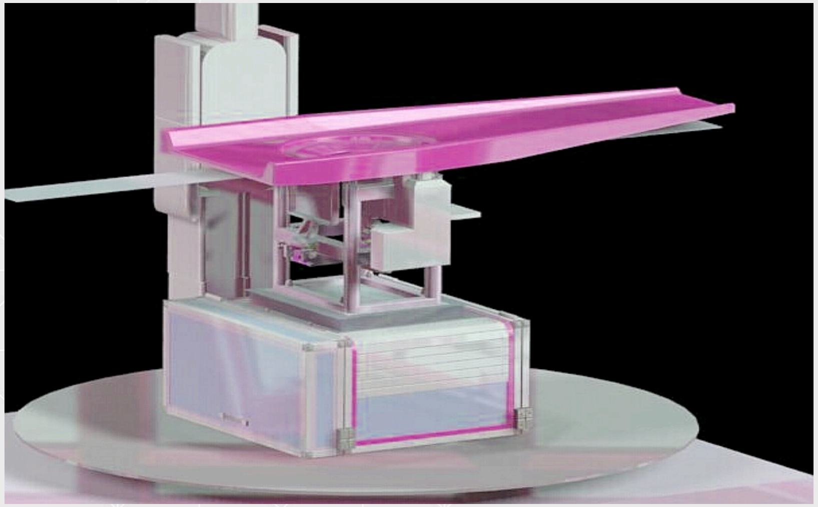
phase contrast

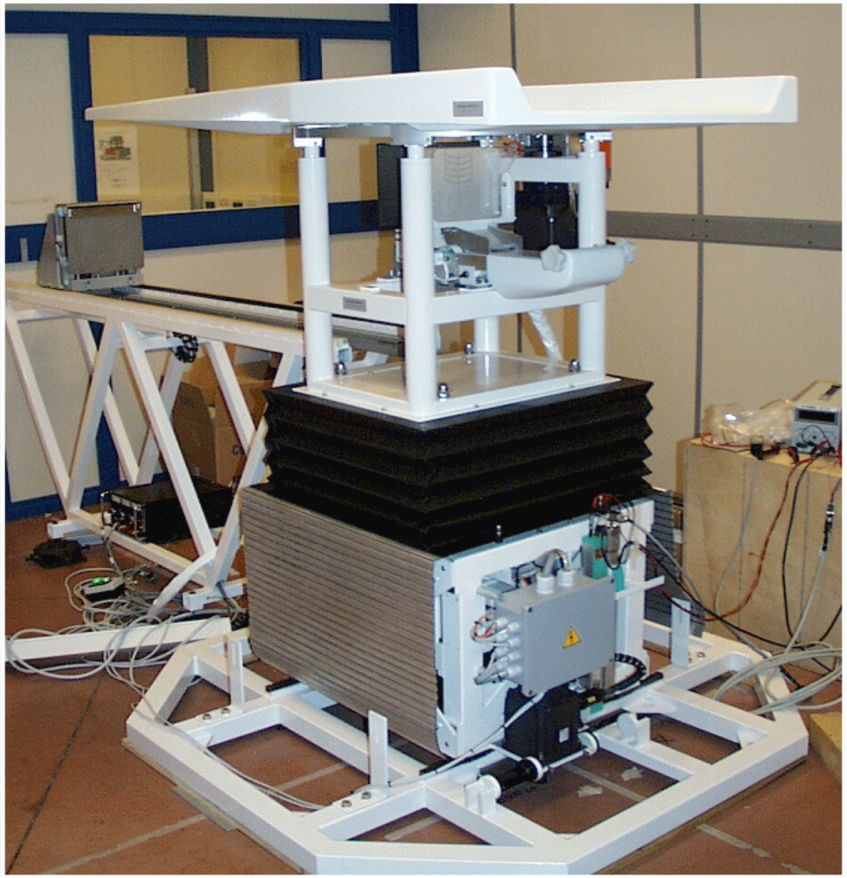


Arfelli et al. Phys. Med. Biol. 43 (1998) 2845-52

Which led to the realization of a dedicated mammography station in TS

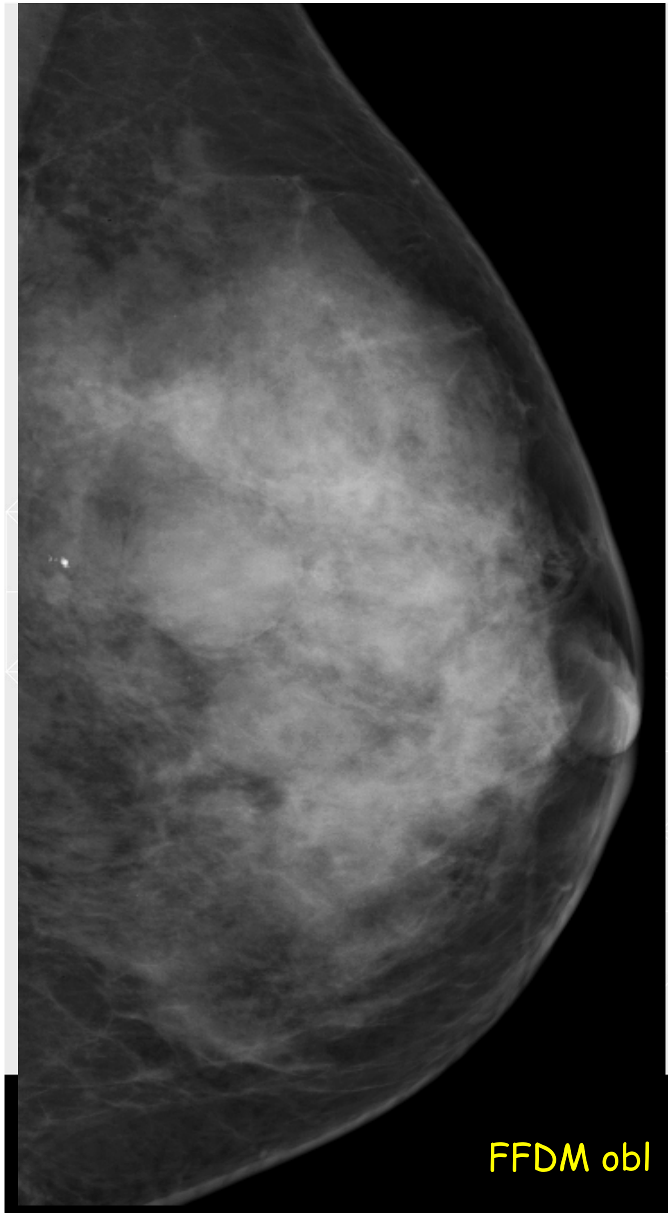


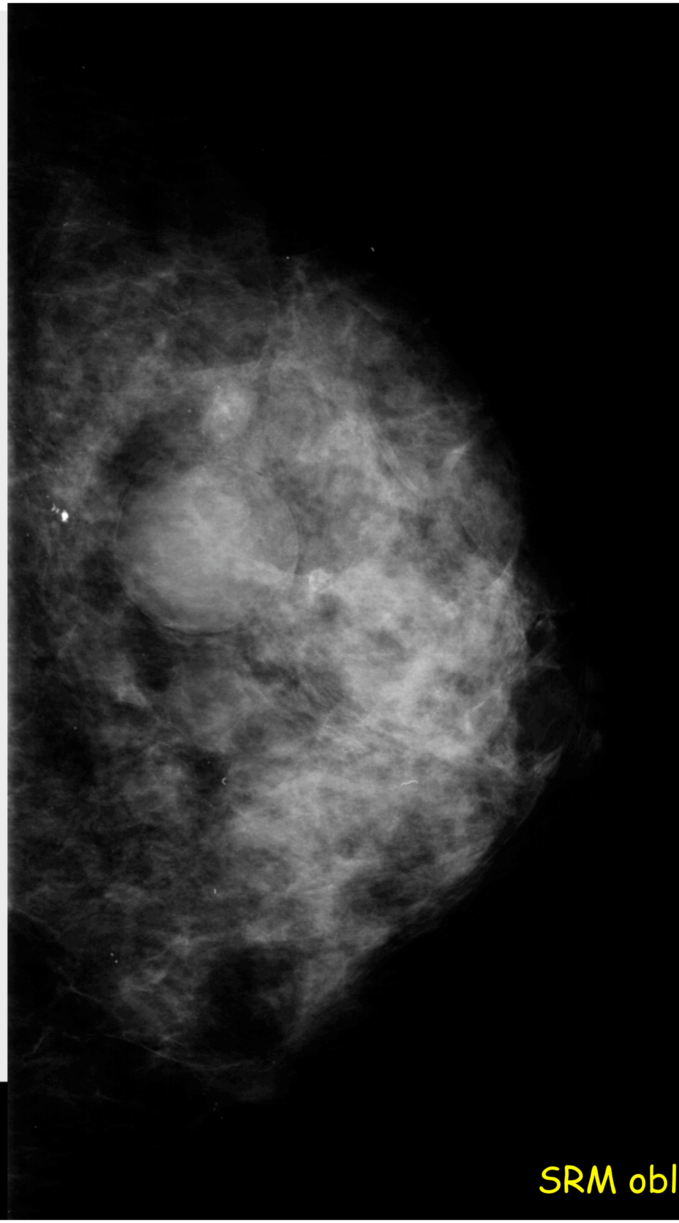




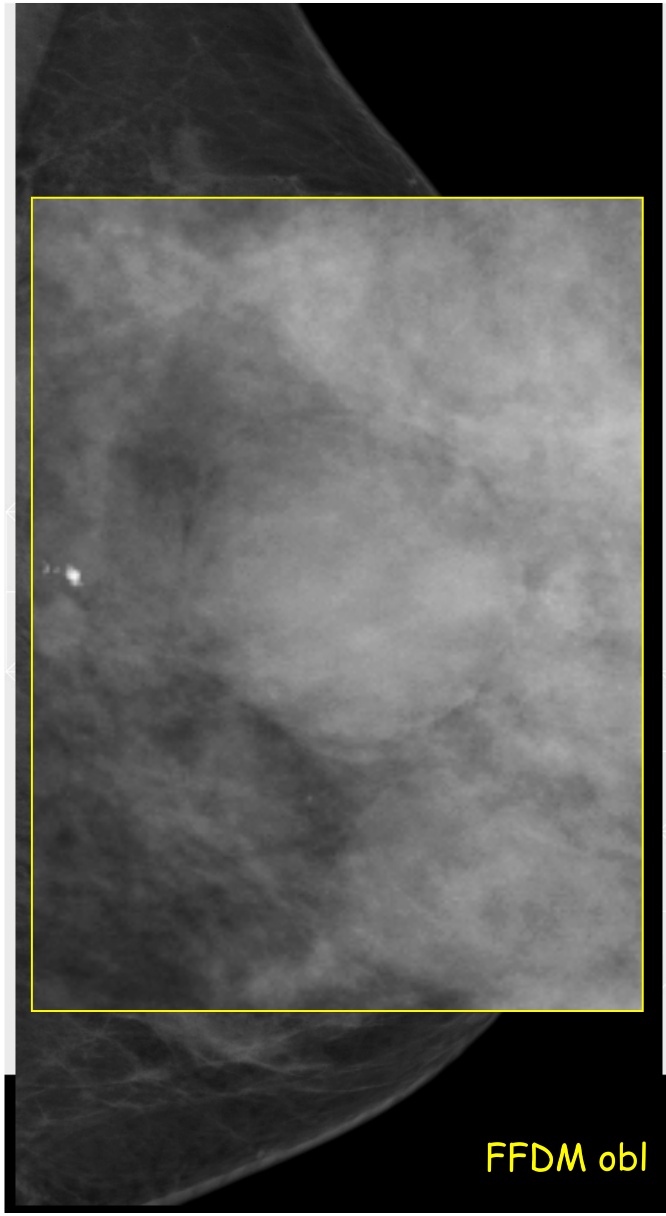
Castelli et al. Radiology 259 (2011) 684-94

SRM: findings

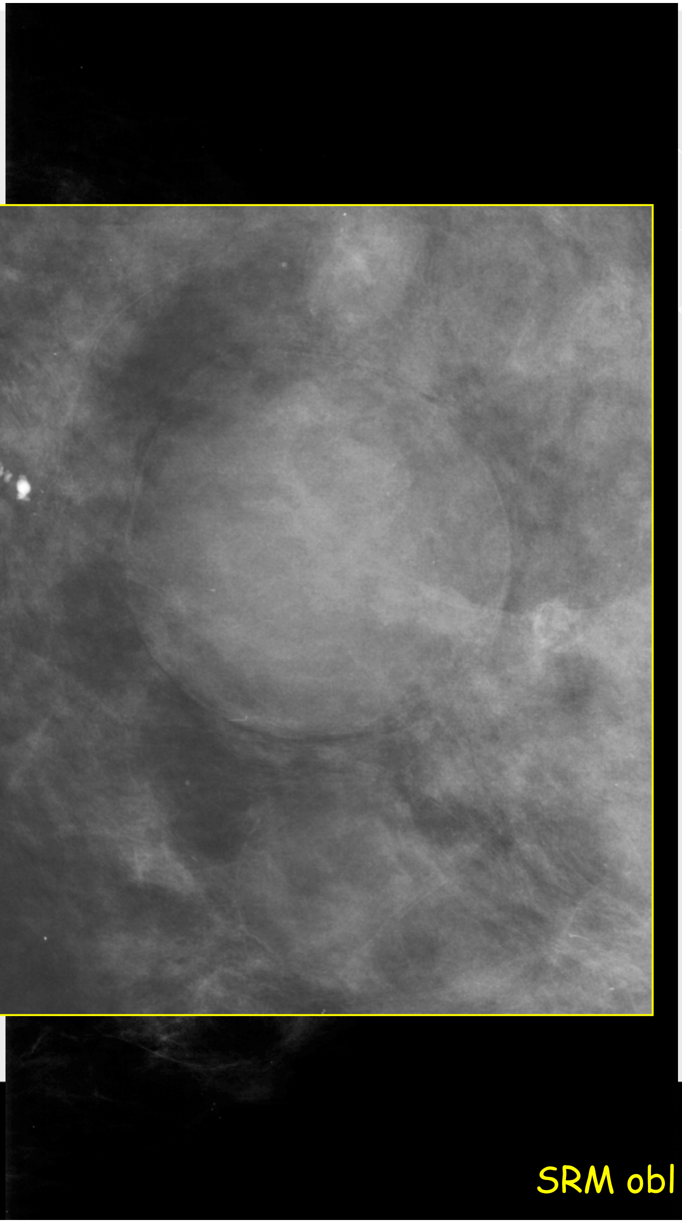




SRM: findings



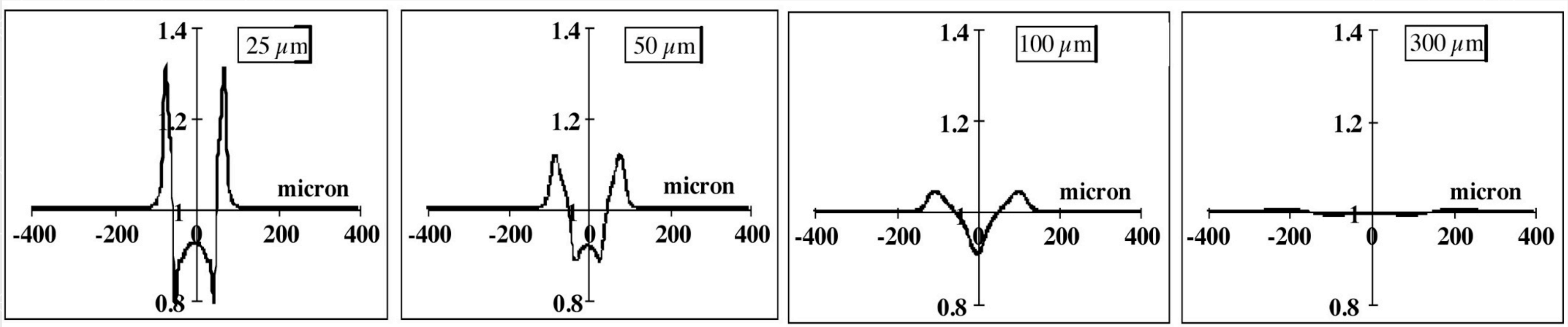
FFDM obl



SRM obl

SO WHAT IS THE PROBLEM?

FSP suffer immensely when transferred to conventional sources:
the spread function discussed previously becomes too large and kills the signal.



Moreover:

The system has little flexibility - only d_{sd} can be changed

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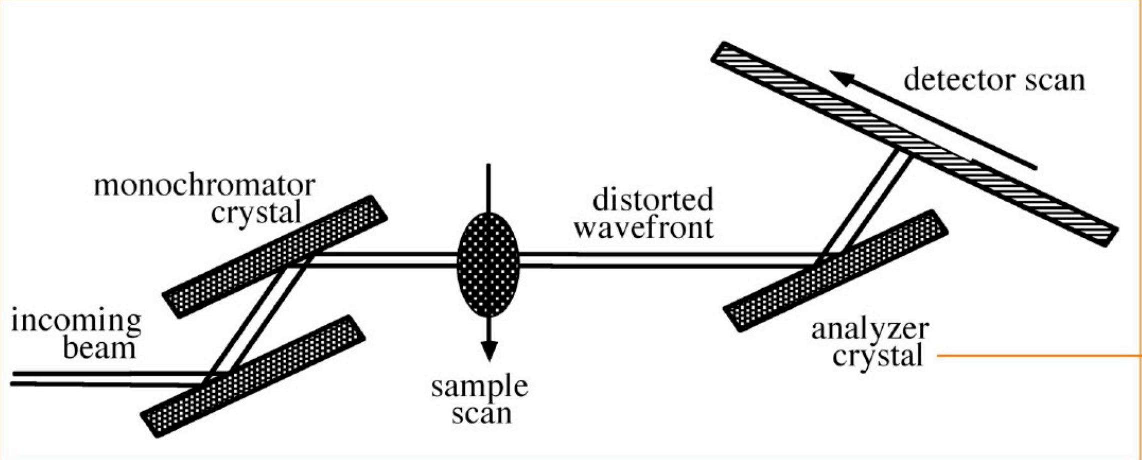
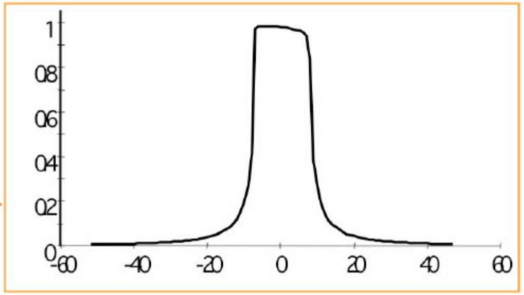
Olivo *et al*. Med. Phys. 28 (2001)1610-19

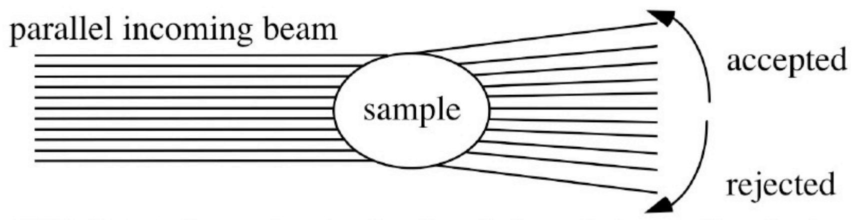
Other methods to perform phase contrast imaging:

"Analyzer Based Imaging"

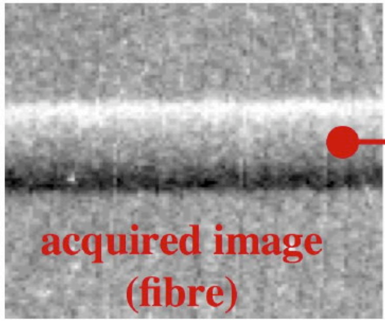




a small misalignment makes it more sensitive:



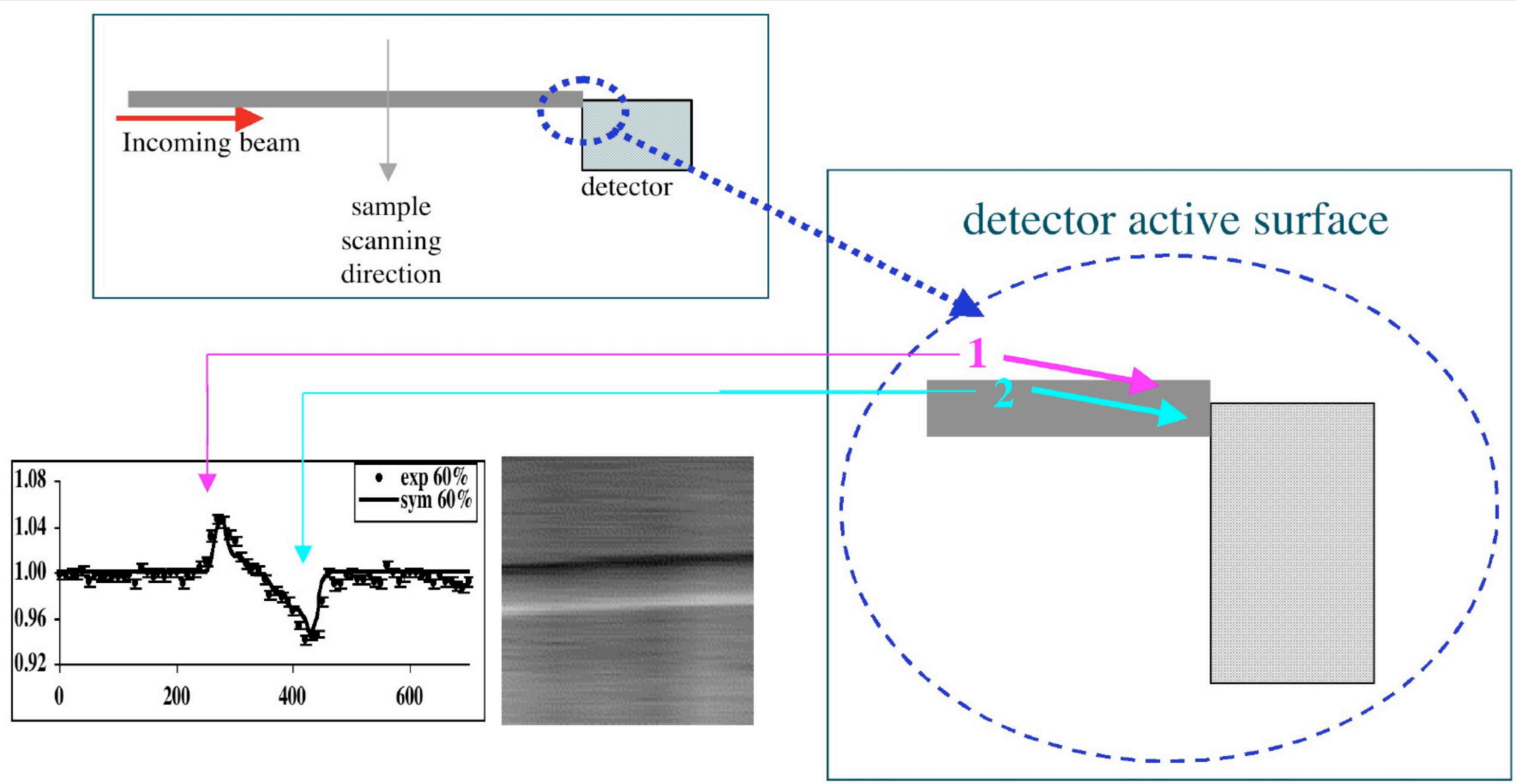
(NB distorted wavefront-> local variation of photon direction)



NOTE: NO ABSORPTION

Davis et al, Nature 373 (1995) 595-8; Ingal & Beliaevskaya, J. Phys. D 28 (1995) 2314-7, Chapman *et al*, Phys. Med. Biol. **42** (1997) 2015-25 - **but even before that Forster 1980!**

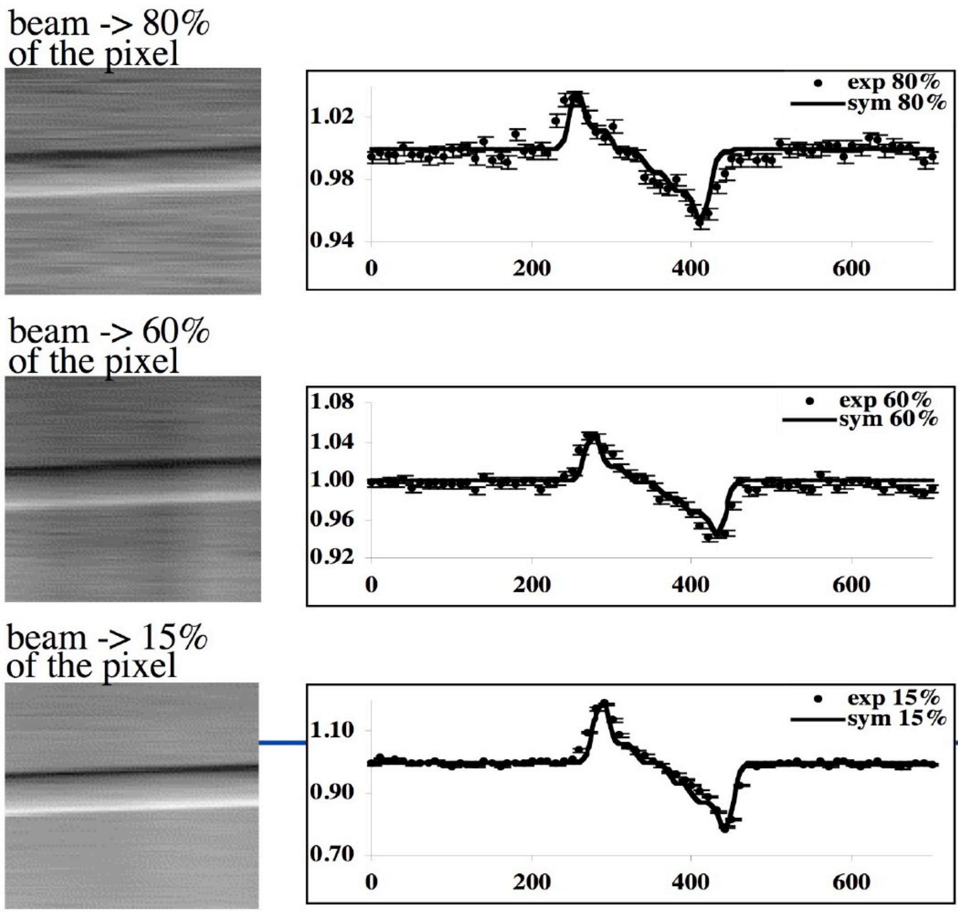
A different way to obtain a similar effect:
The Edge Illumination Technique



Provides results similar to ABI but opens the way to the use of **divergent and polychromatic beams**

Olivo *et al*. Med. Phys. 28 (2001)1610-19

Sensitivity vs. exposed pixel fraction:



Increased sensitivity with reduced beam thickness

N.B. THE VERTICAL SCALE IS NOT THE SAME FOR THE THREE PLOTS

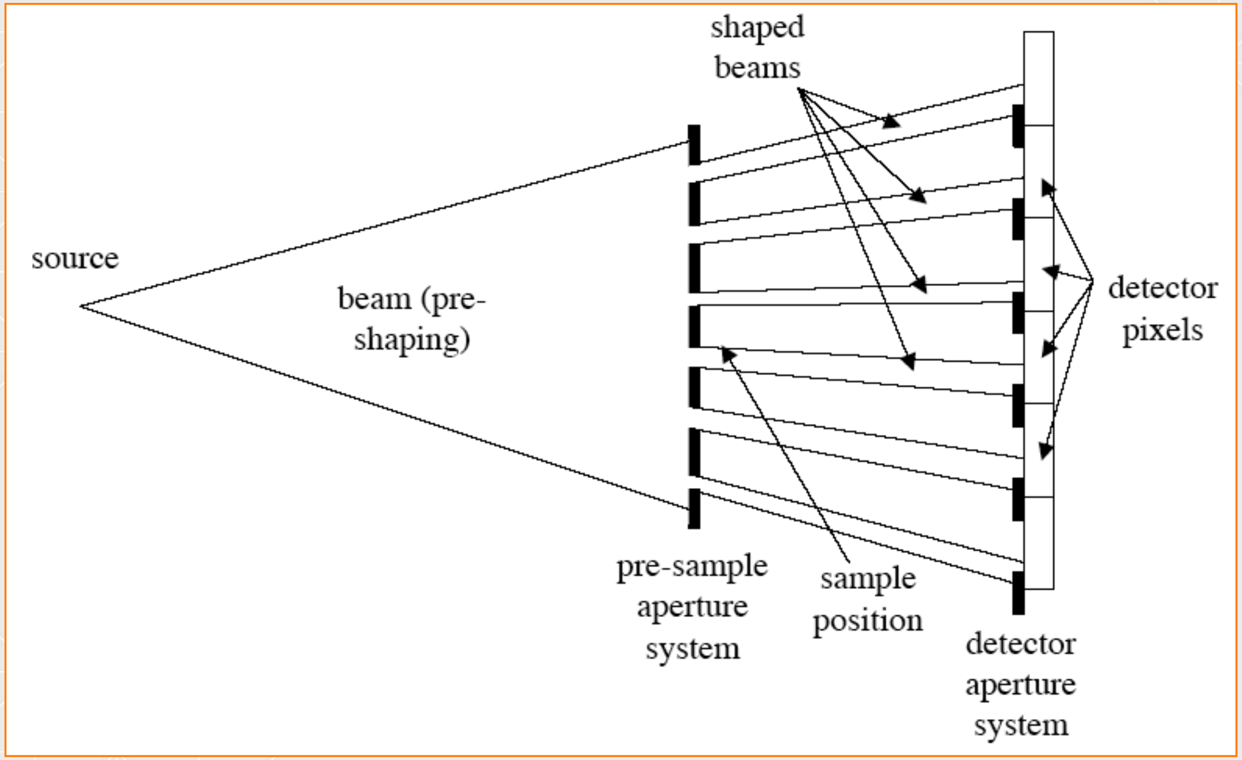
In fact the signal is equal to:

~ 8% (illumination 80%)
~ 12% (illumination 60%)
~ 40% (illumination 15%)

Important consequence on coded-aperture method: you can't calculate sensitivity as pitch/sample-to-detector distance as **it is not a single number**: it depends on the mask position (more later)

Olivo *et al.* Med. Phys. 28 (2001)1610-19

THE METHOD CAN THEN BE ADAPTED TO A DIVERGENT AND POLYCHROMATIC (=conventional) SOURCE

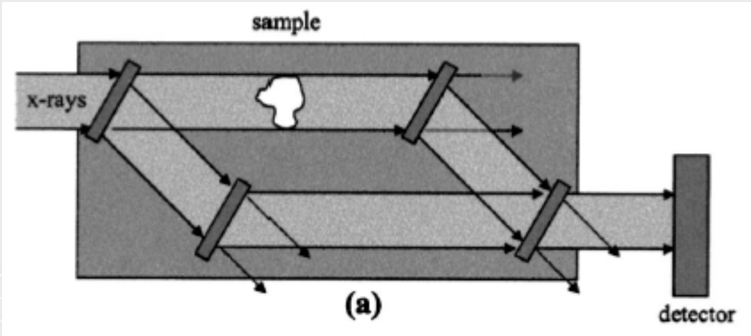


NB for those of you who are familiar with grating (or Talbot, or Talbot-Lau) interferometers **this isn't one!**

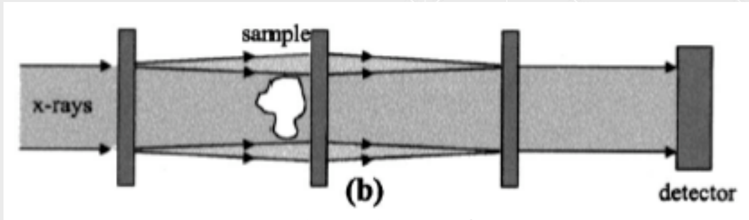
Olivo and Speller Appl. Phys. Lett. 91 (2007) 074106

interlude:

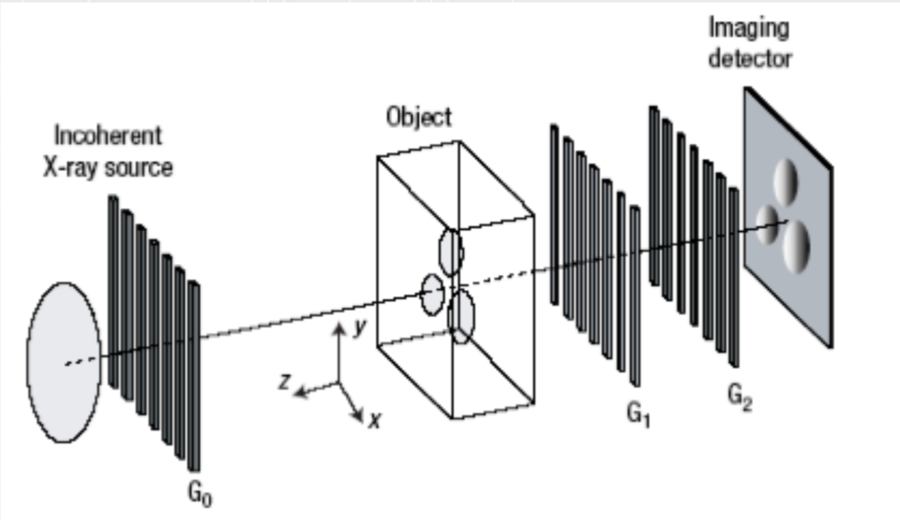
The TALBOT/LAU interferometer

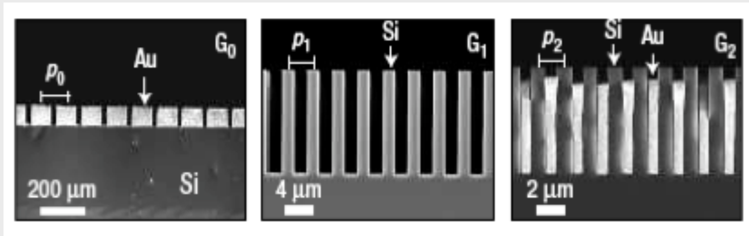


The classic, "Bonse-Hart" interferometer



The shearing interferometer





The used gratings, obtained through microfabrication techniques

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Synchrotron: David et al APL 81 (2002) 3287-9, Momose et al Jpn J Appl Phys 42 (2003) L866-8; Lab source Pfeiffer *et al*, Nature Physics **2** (2006) 258-61

My concerns with the Talbot/Lau approach:

- exposure times are increased:

in particular by the limited angular acceptance of the gratings - let's not forget that the beam is divergent!
(let's leave aside the phase stepping "problem" for the moment)

- the technique does not work with fully polychromatic beams:

a maximum bandwidth ~5-10% can be tolerated -> the spectrum produced cannot be fully exploited

- the sensitivity to environmental vibrations is reduced with respect to crystal-based methods but not eliminated:

the detector grating has a 2 μm pitch -> required tolerance pitch/10 (Weitkamp *et al*, 2005),
plus phase stepping -> tens of nm (!) (Zambelli et al, 2010)

- dose is delivered inefficiently:

detector grating ->50% fill-factor, + absorption in Si (40% through 1x300 μm wafer, 60% through 2 wafers)

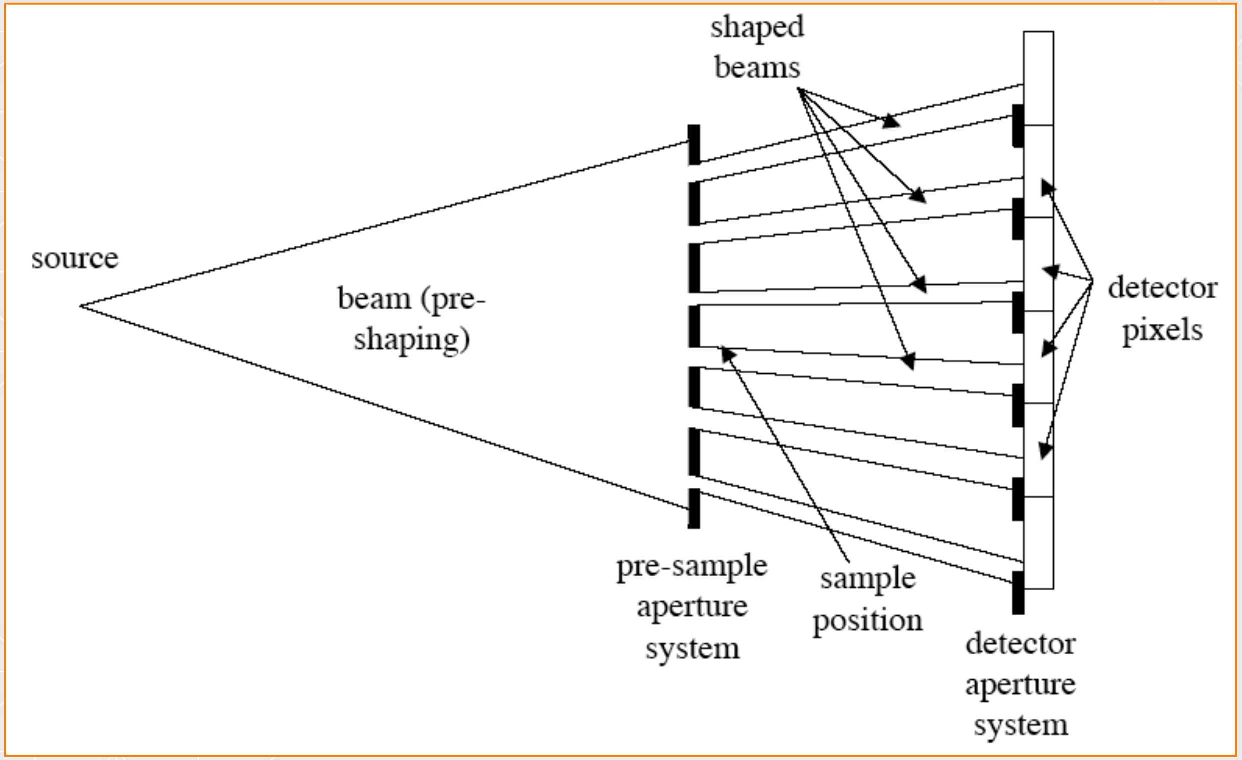
- the field of view is currently limited to ~6x6 cm^2

by the micro-fabrication process involved, which prevents the realization of larger gratings

-the technique is sensitive to phase effects in one direction only:

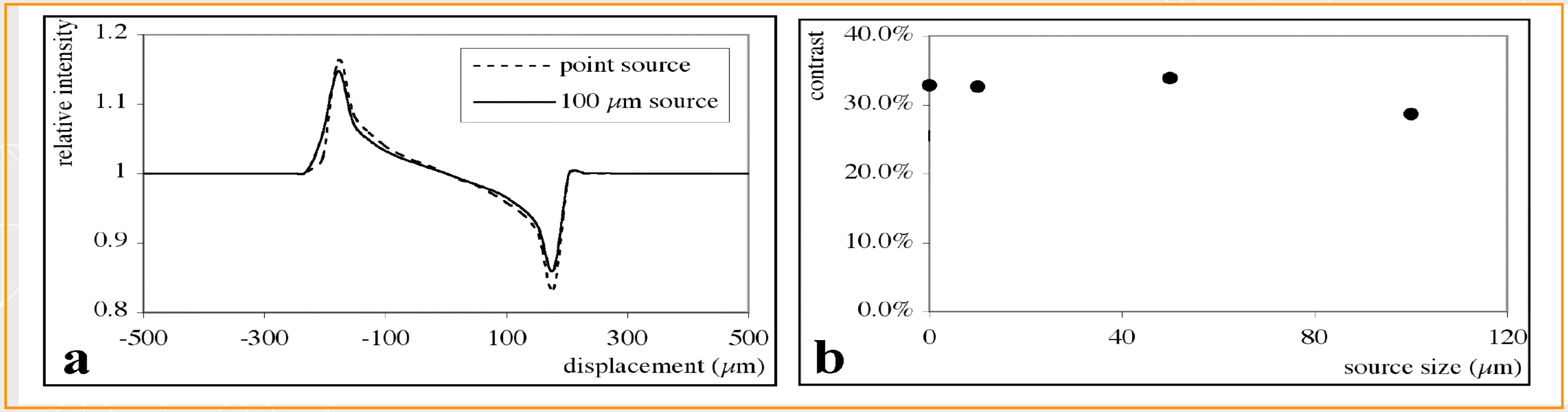
without featuring the flexibility of ABI

BACK TO EDGE ILLUMINATION



Olivo and Speller Appl. Phys. Lett. 91 (2007) 074106

Little loss of signal intensity for source sizes up to 100 µm



Which can be achieved with state-of-the-art mammo sources

Why?

1) Because we are only relying on refraction, which survives under relaxed coherence conditions;
2) Because we are use aperture pitches matching the pixel size, i.e. BIG: the projected source size remains < pitch, and therefore blurring does "not" occur.

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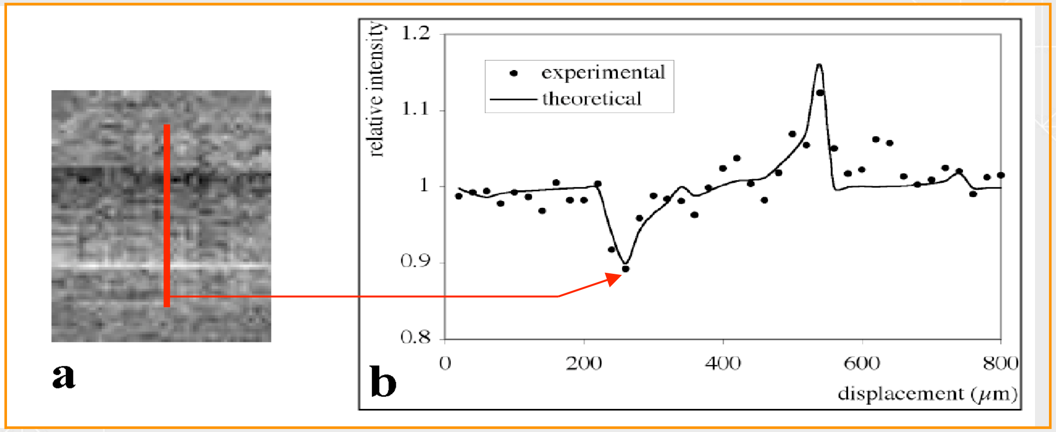
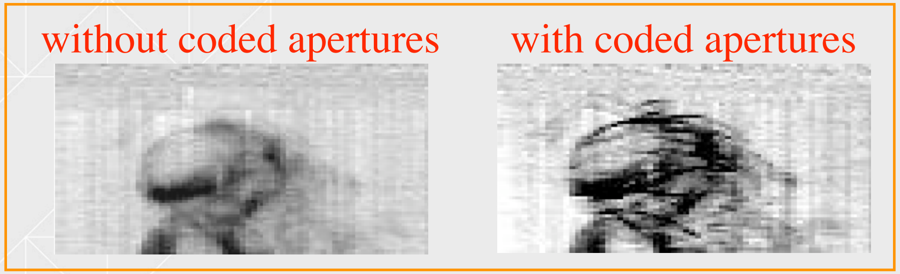
Olivo and Speller Phys. Med. Biol. 52 (2007) 6555-73

Proof-of-concept results



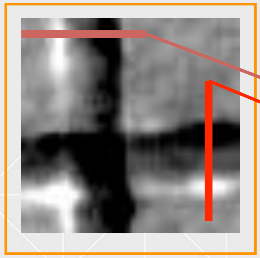
NB absorption contrast of the fibre ~1% -> 24-fold increase obtained, comparable with SR results. A 100 μm focal spot, divergent and polychromatic source was used.



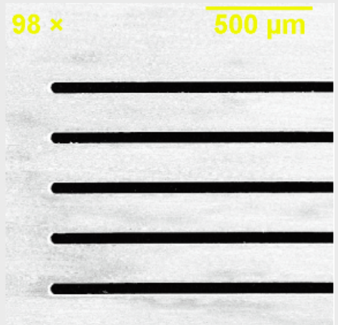
Coded-aperture XPCi can thus be done in a laboratory

Olivo and Speller Appl. Phys. Lett. 91 (2007) 074106

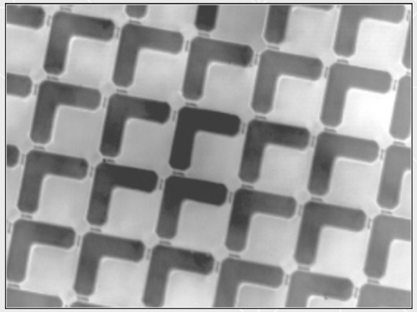
2D-sensitivity:

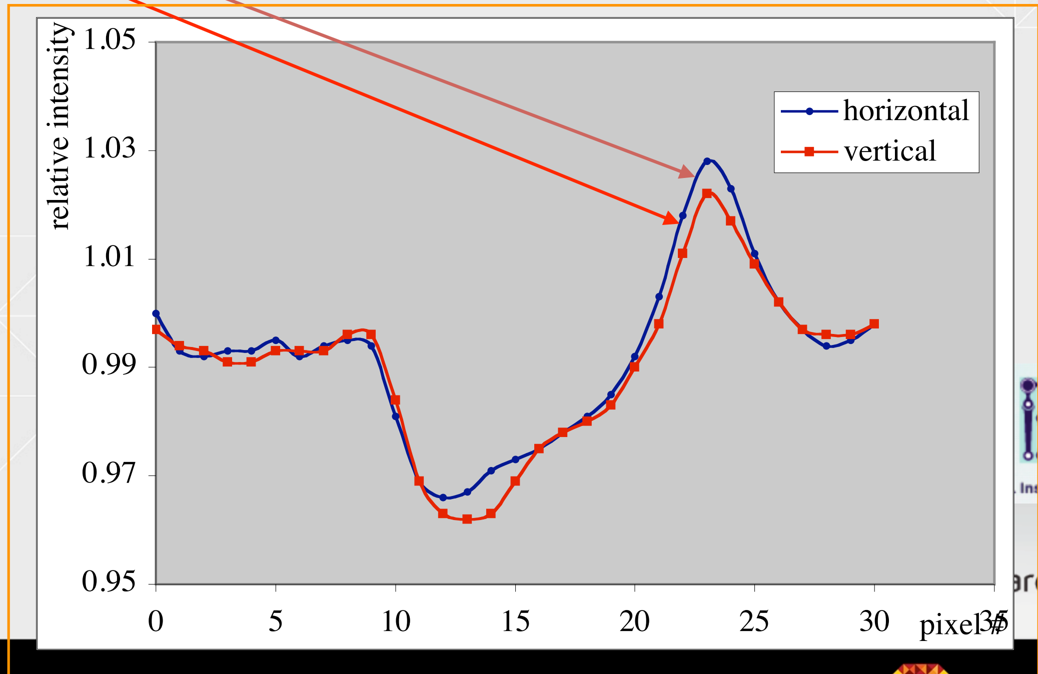


from:



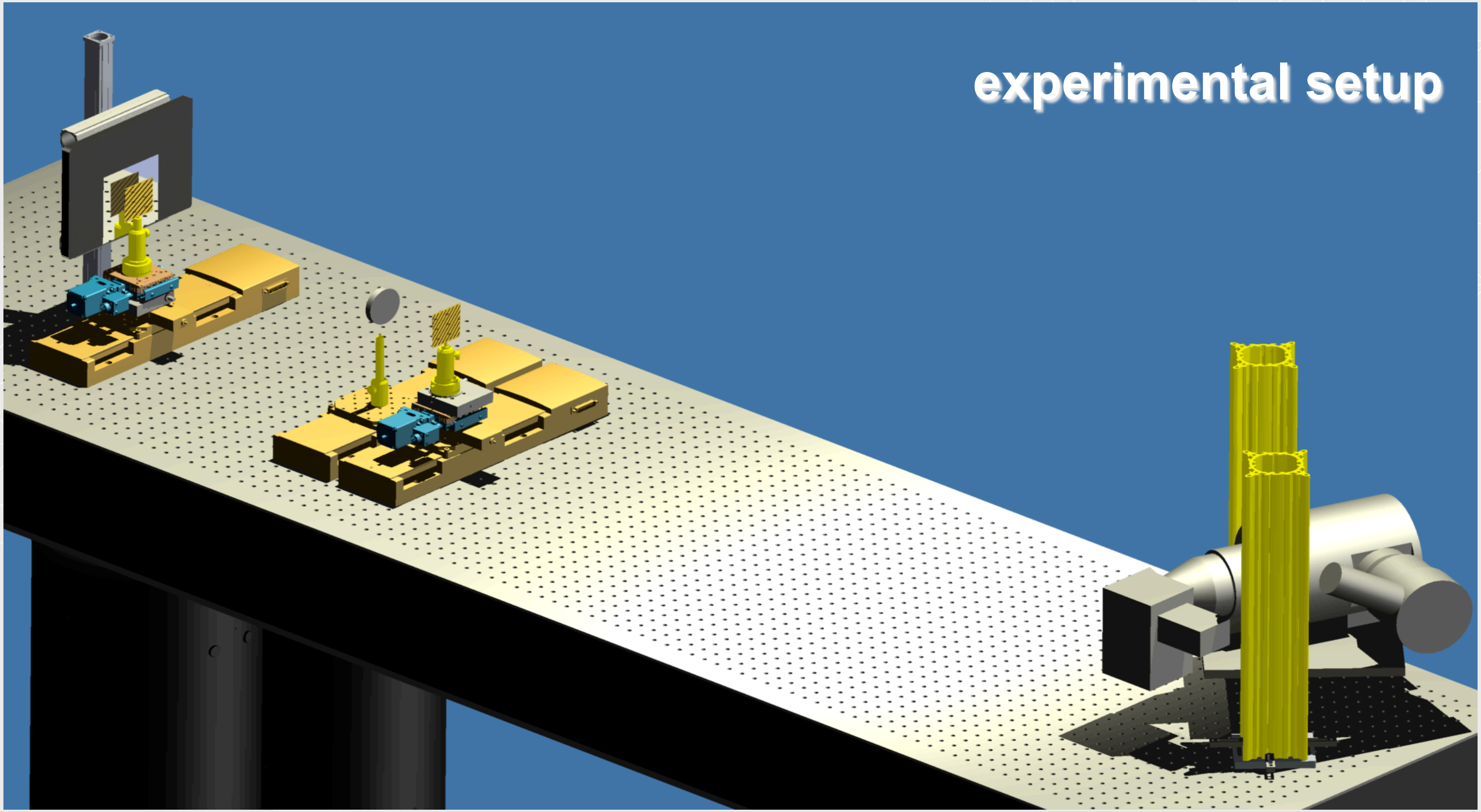
to





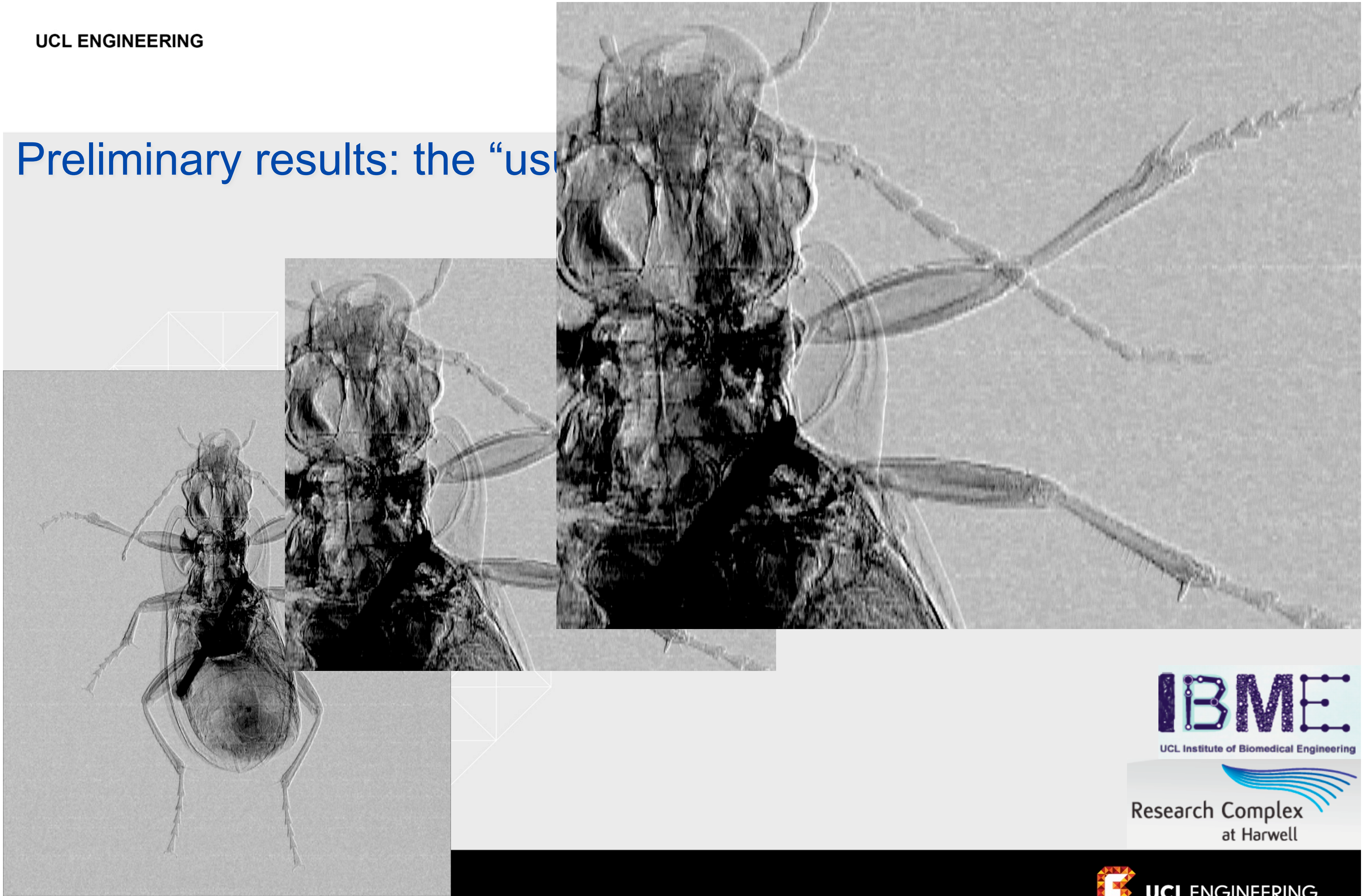
Olivo *et al* Appl. Phys. Lett. 94 (2009) 044108

experimental setup

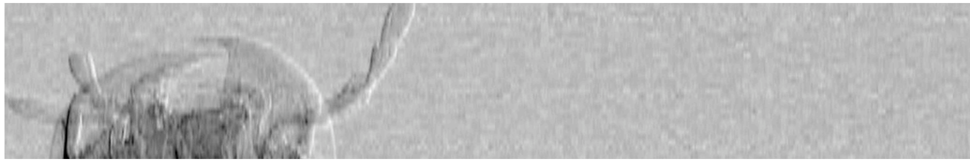


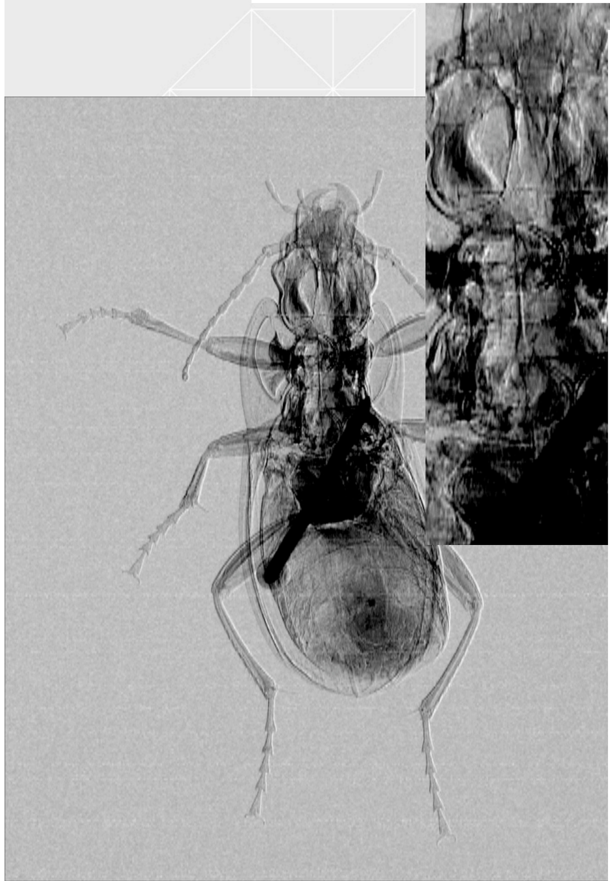
experimental setup

Preliminary results: the “us



Prelimir





RESEARCH HIGHLIGHTS

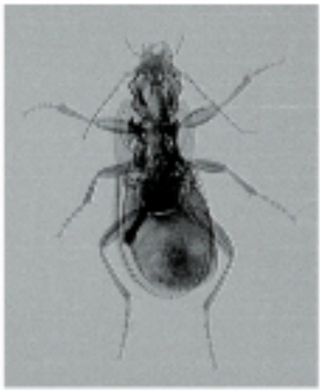
Selections from the scientific literature

APPLIED PHYSICS

Better X-ray vision

A new technique allows fainter features to be imaged by X-rays.

Conventional X-ray imaging relies on the absorption and scattering of X-ray photons by the object being imaged. But X-ray phase-contrast imaging instead detects changes in the photons' direction and velocity.

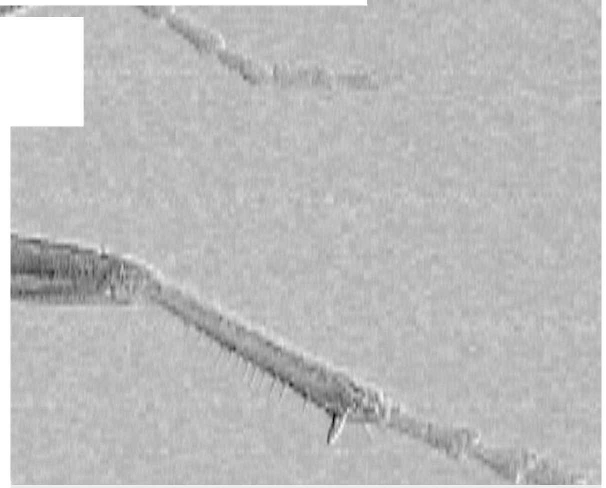


A. OLIVO ET AL.

Alessandro Olivo and his colleagues at University College London used a conventional X-ray source outfitted with grated masks — one in front of the object for imaging and one behind it. The masks were offset slightly from one another so that they filtered out some of the photons, reducing background noise. The detector measures by how much photons have deviated from their path, capturing different image data from conventional X-ray imaging and boosting the visibility of fine detail.

The team used its technique to image biological specimens such as a beetle (pictured), as well as samples of interest for medical imaging, materials science and security inspection.

Appl. Optics 50, 1765–1769 (2011)



Nature 472 (2011) p. 392

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ADVANCES

PHYSICS

Can You See Me Now?

A new x-ray technique may herald improved baggage screening and mammograms

X-rays can help reveal anything from bombs hidden in luggage to tumors in breasts, but some potentially vital clues might be too faint to capture with conventional methods. Now a new x-ray technique adapted from atom smashers could resolve more key details.

Conventional x-ray imaging works much like traditional photography, relying on the light—in this case, x-rays—that a target absorbs, transmits and scatters. To make out fine details, one typically needs a lot of x-rays, either over time, which can expose targets to damaging levels of radiation, or all at once from powerful sources such as circular particle accelerators, or synchrotrons, which are expensive.

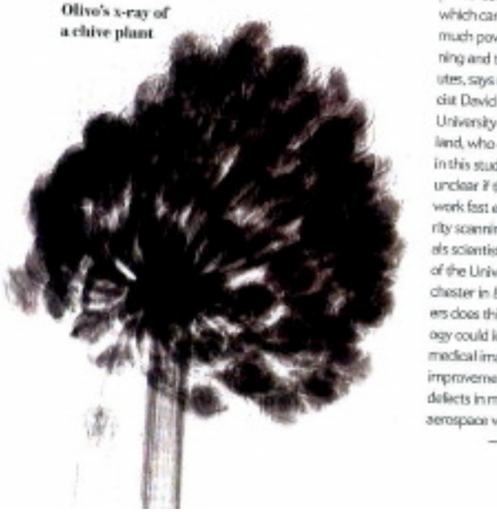
Instead physicist Alessandro Olivo of University College London and his colleagues suggest imaging an object by looking for very small deviations in an x-ray's direction as it moves through that object. Their idea is to take such x-ray phase-contrast imaging, which has been used in synchrotrons for more than 15 years, and use it with conventional x-rays.

The scientists rig conventional x-ray sources with gold grates that are 100 microns or so thick—one in front of a target and one behind it. The holes on one grate do not line up exactly with the holes on the other, meaning x-rays that passed in straight lines through the first grate would get filtered out by the second, lowering background noise. The detector then analyzes only the photons that deviated in direction as they passed through the object. This can lead to at least 10 times greater contrast than conventional imaging—"all details are more clearly visible, and details classically considered very hard to detect become detectable," Olivo says of findings reported recently in *Applied Optics*. Whereas bombs are usually visible in conventional x-ray imaging, they can be confused with other materials such as plastics or liquids. The scientists are now pushing imaging sensitivity even further with new grating designs and are working on 3-D scanning techniques by coming at the target from multiple angles.

This system can generate images in just seconds, far quicker than other x-ray phase-contrast techniques, which cannot exert as much power during scanning and thus require minutes, says radiation physicist David Bradley of the University of Surrey in England, who did not take part in this study. But it remains unclear if this system could work fast enough for security scanning, says materials scientist Philip Withers of the University of Manchester in England. Withers does think the technology could lead to better medical imaging, as well as improvements in detecting defects in materials used in aerospace work.

—Charles Q. Choi

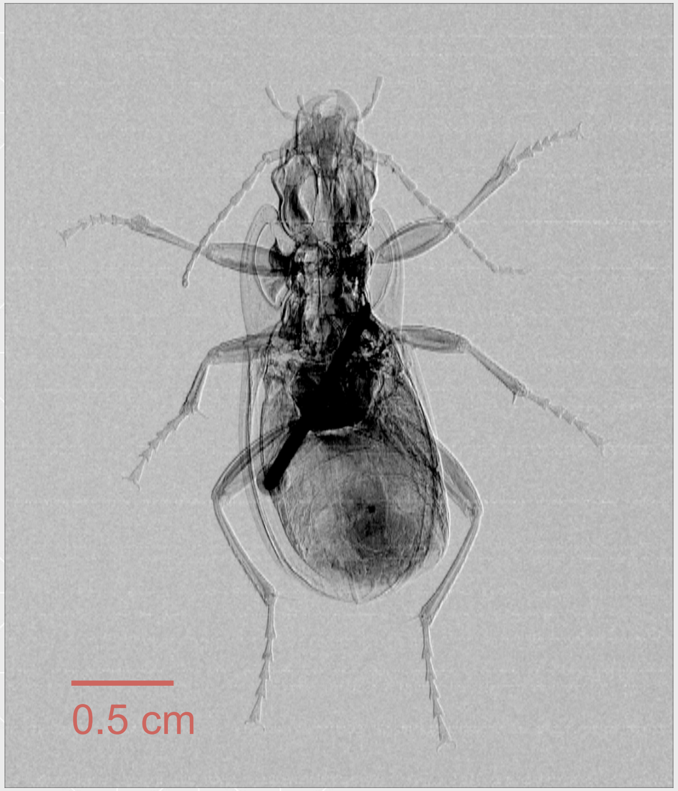
Olivo's x-ray of a chive plant



Scientific American 305 (2011) p. 14

How fast does "faster" mean?

~ 1' exposure



6s exposure

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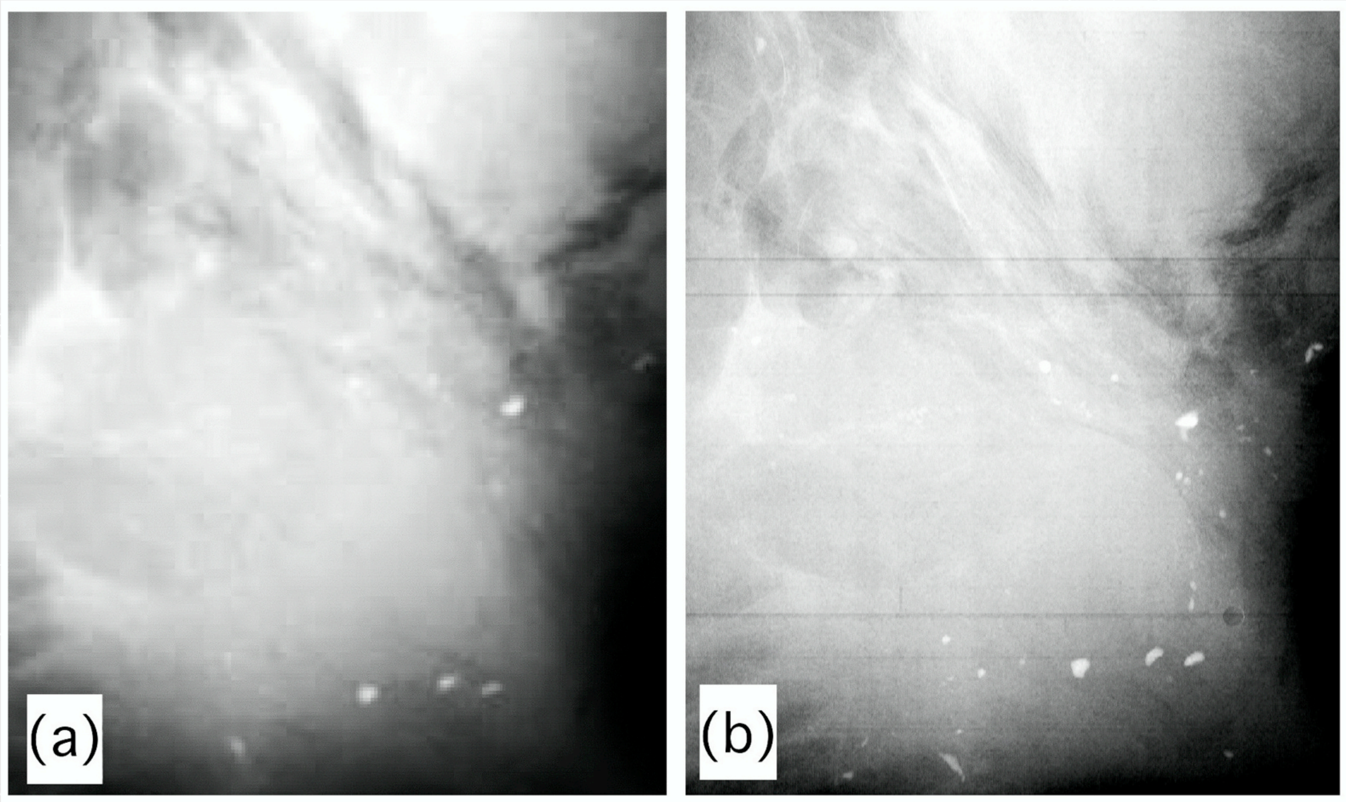
Preliminary results - mammo



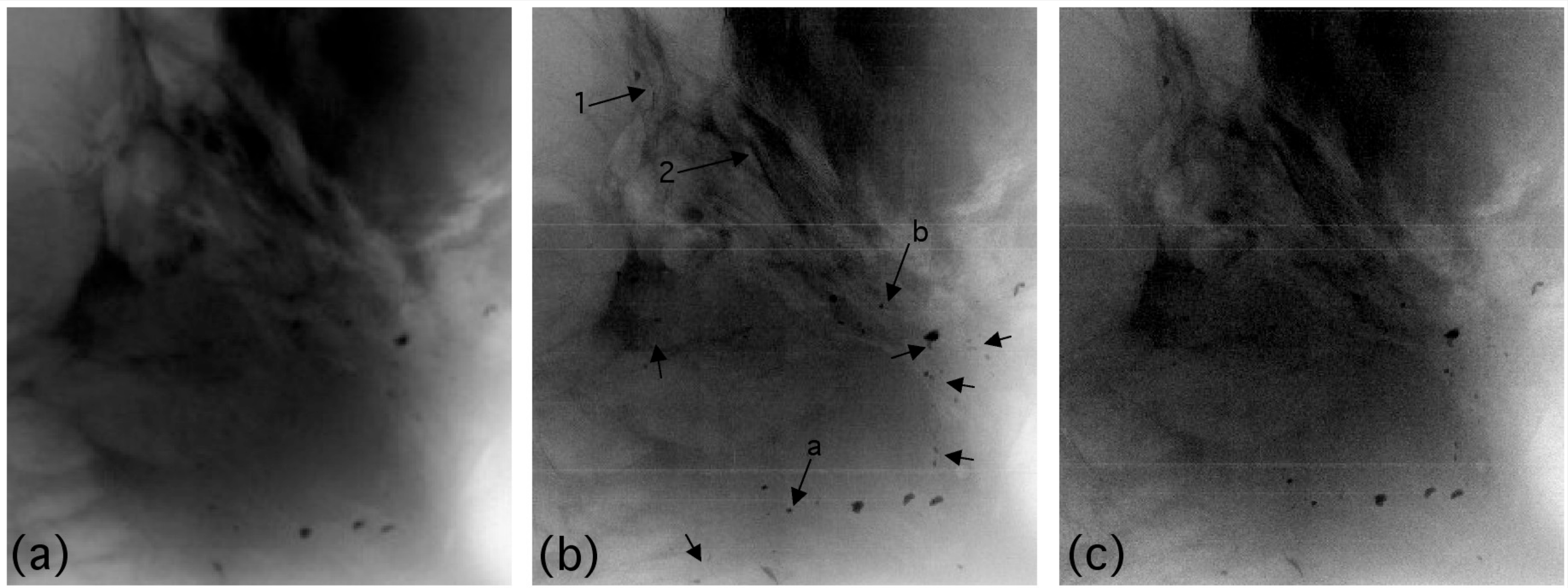
(a): GE senographe Essential ADS 54.11; 25 kVp, 26 mAs

(b): coded-aperture XPCi, 40 kVp, 25 mA – **ENTRANCE** dose 7 mGy (< mammo!)

It has to be said the tissue was 2.5 cm thick -> we expect ~ same dose for thicker tissues

Olivo et al Med. Phys. 40 (2013) 090701

Preliminary results - mammo



1.5 mGy (conventional)

3 mGy (XPCi)

0.7 mGy (XPCi)

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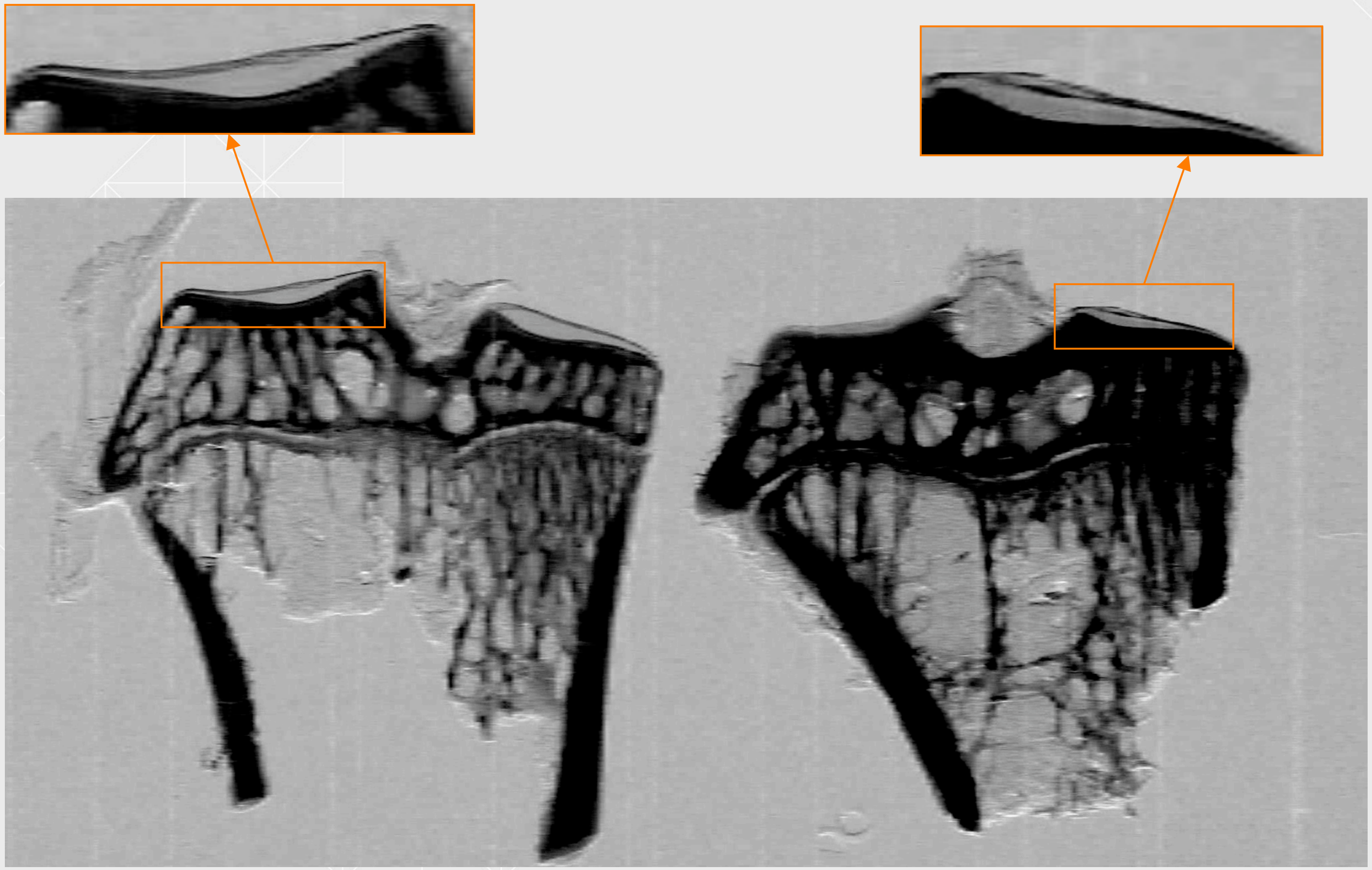
Olivo et al Med. Phys. 40 (2013) 090701

Preliminary results - cartilage imaging

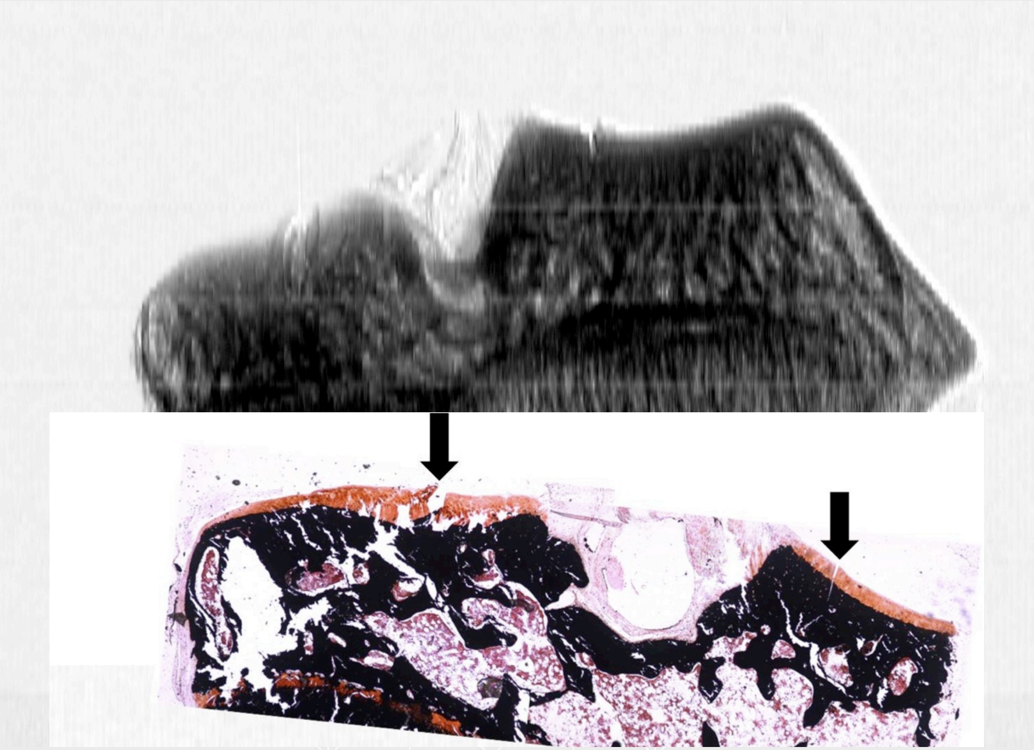
Rat cartilage, ~ 100 μm thick, invisible to conventional x-rays



Marenzana *et al*, Phys. Med. Biol. 57 (2012) 8173-84

Preliminary results - cartilage imaging

XPCi

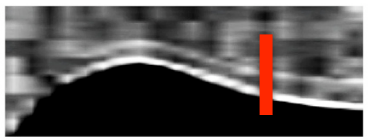


Abs

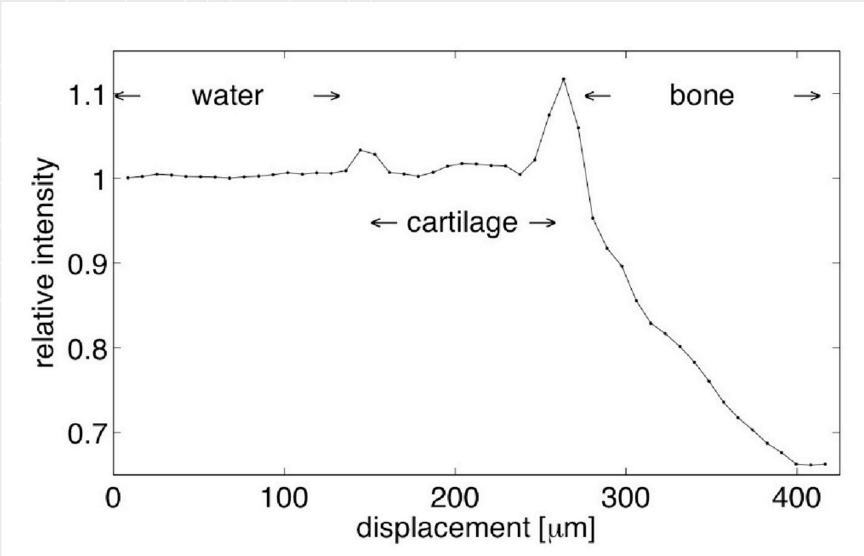
Marenzana *et al*, Phys. Med. Biol. 57 (2012) 8173-84

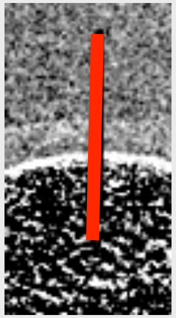
Cartilage in water:

Tells us a lot about CAXPCi vs Talbot/Lau sensitivity:



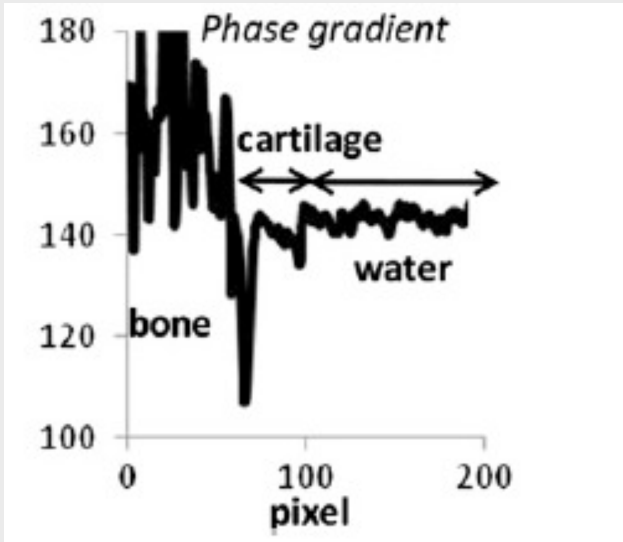
CAXPCI
(RAT cartilage)





TALBOT/LAU
(PORK cartilage)

from Stutman *et al*, Phys. Med. Biol. 56 (2011) 5697-720



- SAME signal (despite thicker cartilage for T/L);

- on **3rd** Talbot order (cartilage in water invisible on 1st order)

Marenzana *et al*, Phys. Med. Biol. 57 (2012) 8173-84

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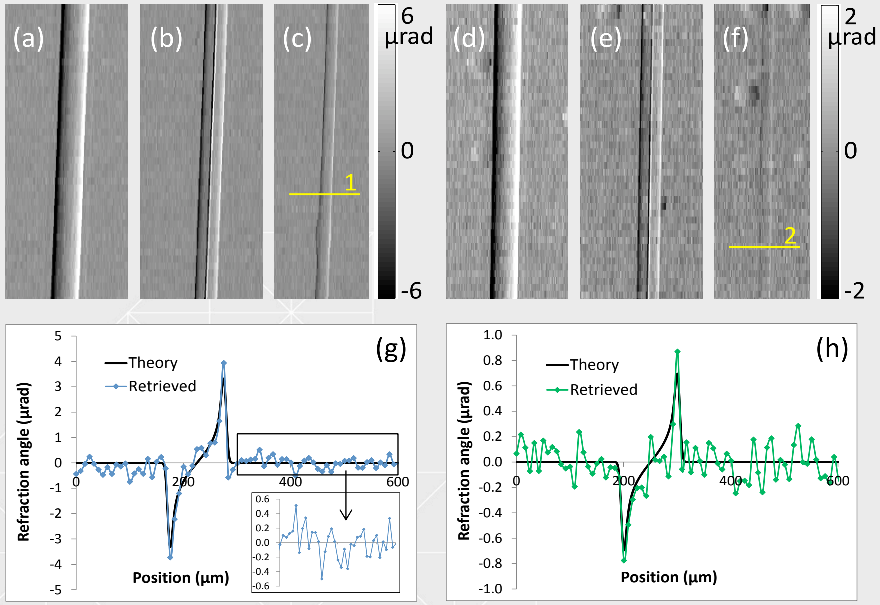
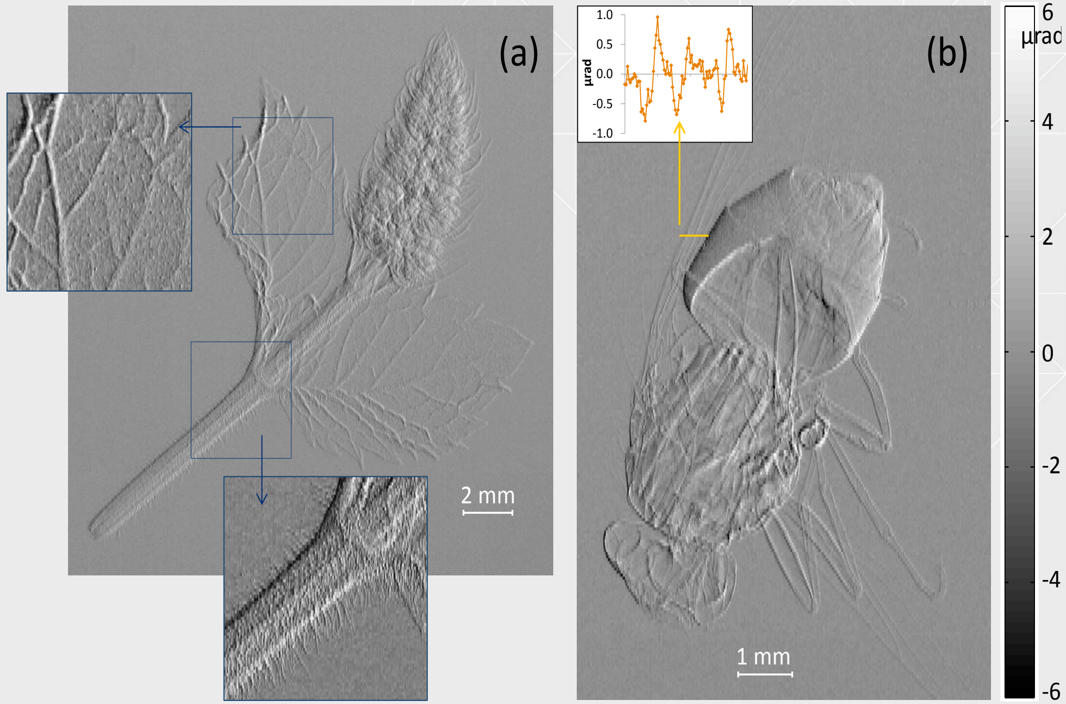
More on the sensitivity of the lab system:





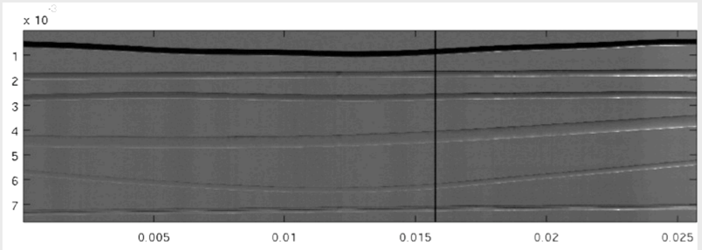
$$\Delta\theta_{x,eff} = \frac{1}{z_{od}} R^{-1}\left(\frac{I_{obj,+}}{I_{obj,-}}\right) \rightarrow \sigma\left(\Delta\theta_{x,eff}\right); \frac{\sqrt{C\left(x_{e,+}\right)}}{z_{od}\sqrt{2TI_0}\left[\rho_{ref,n}\left(x_{e,+}\right)-\rho_{ref,n}\left(x_{e,+}+d\right)\right]}$$

This gives a phase sensitivity of ~ 270 nRad, with only 2 images x 7s exposure each; same as reported by Thuring (Stampanoni's group) for GI. Revol reported a sensitivity of about 110 nRad but with 12 x 7s frames – as one can expect the value to scale with sqrt(exp time), that also fits.

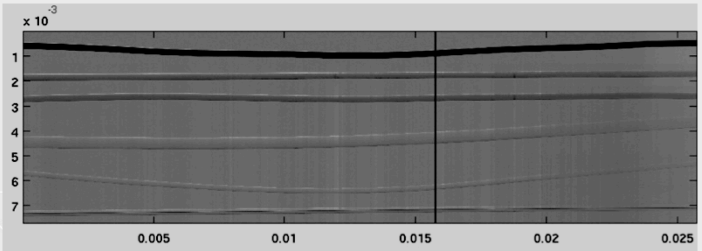
Diemoz *et al*, Appl. Phys. Lett., under review;
Thuring et al Proc. SPIE 8668 (2013) 866813, Revol et al Rev. Sci. Instrum 81 (2010) 073709

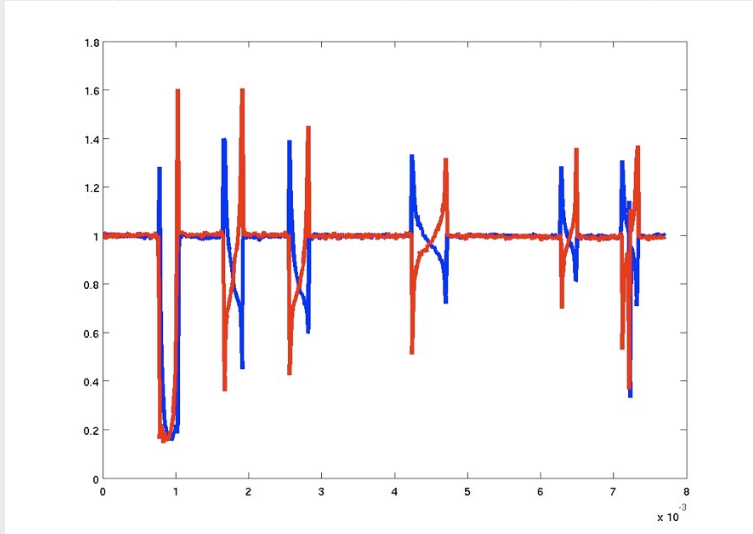
Quantitative phase contrast imaging

“SLOPE -”

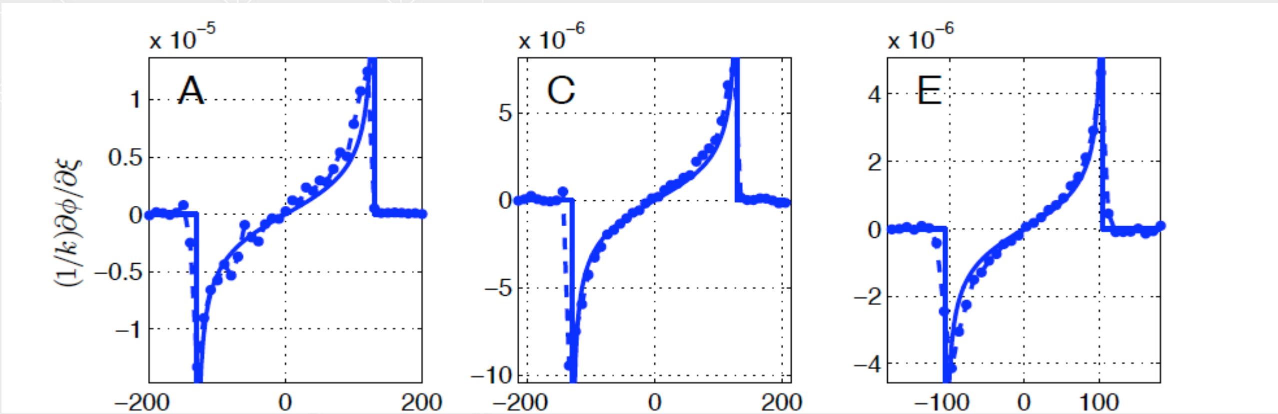


“SLOPE +”





Titanium Aluminum PEEK

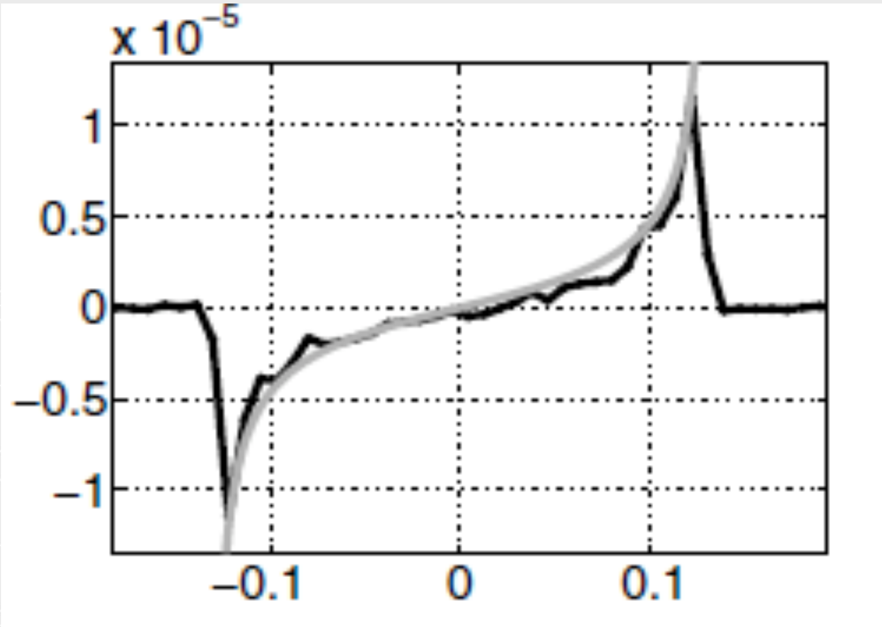


Highly precise retrieval, for both high and low Z materials, up to high gradients where other methods break down

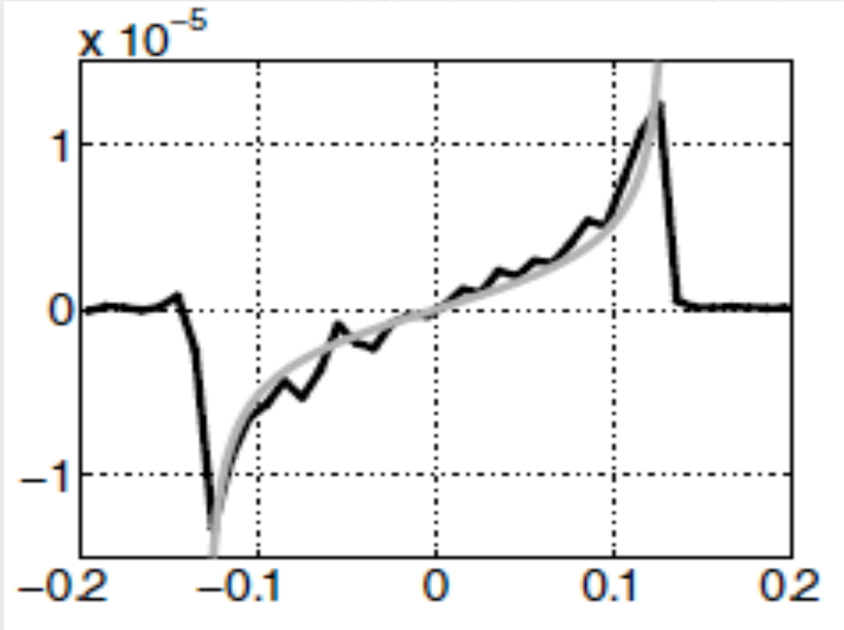
Munro *et al* Opt. Exp. 21 (2013) 647-61

Phase retrieval with synchrotron and conventional sources:

Ti filament: retrieved @ synchrotron



and with conventional source!



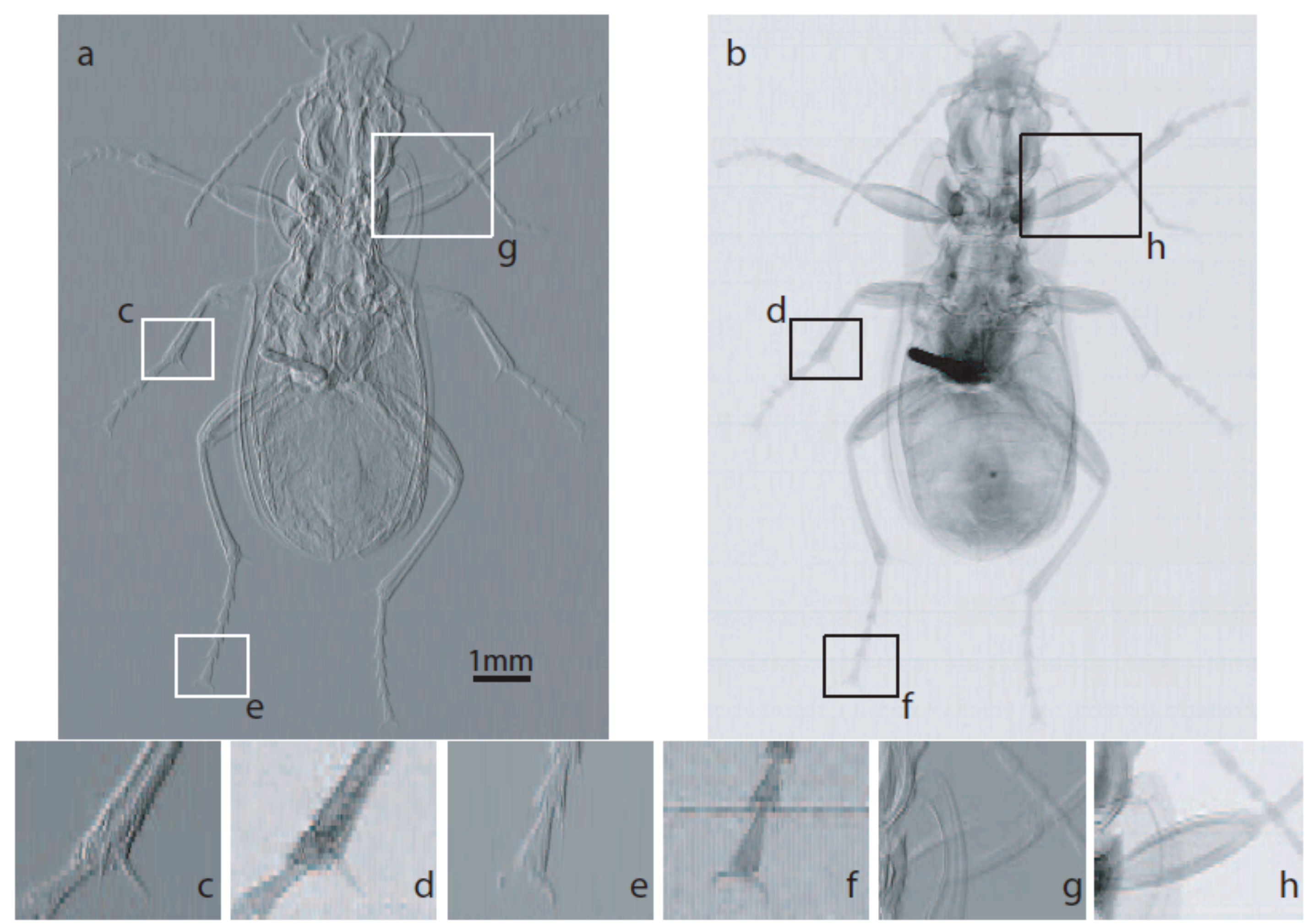
@ conventional source: incoherence modelled as beam spreading – the movement of the "spread" beam is then tracked and referred back to the phase shift that caused it.

But with lots of care as far as "effective energy" is concerned!

(See Munro & Olivo Phys. Rev. A **87** (2013) 053838)

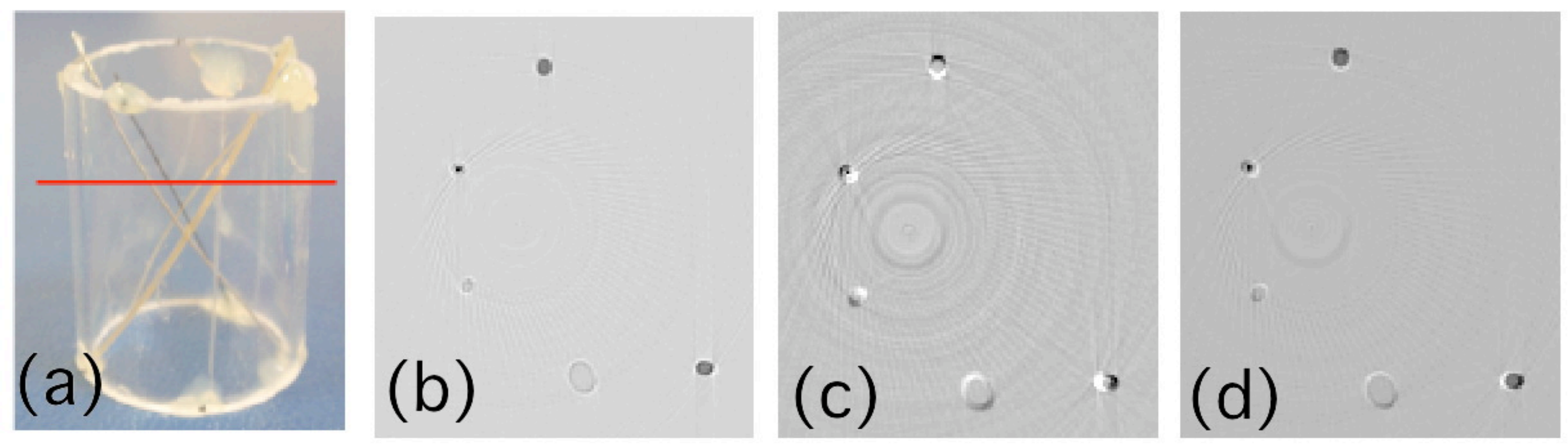
P. Munro *et al*, *PNAS* 109 (2012) 13922-7

Quantitative phase contrast imaging



P. Munro *et al*, *PNAS* 109 (2012) 13922-7

Quantitation -> CT is possible



a) phantom
b) absorption
c) $\vec{\nabla}\Phi$ (integrated version also available)
d) "mixed" (see Diemoz et al Opt. Exp. 19 (2011) 1691-8)

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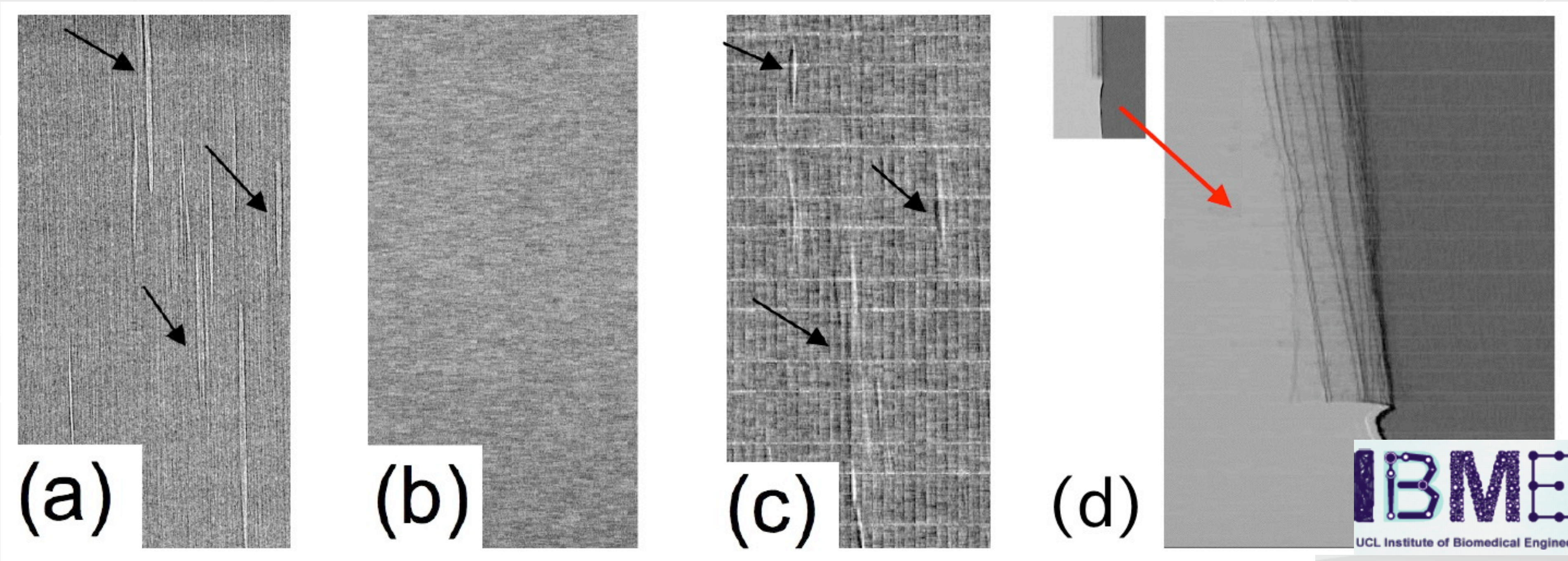
UCL Institute of Biomedical Engineering

Research Complex at Harwell

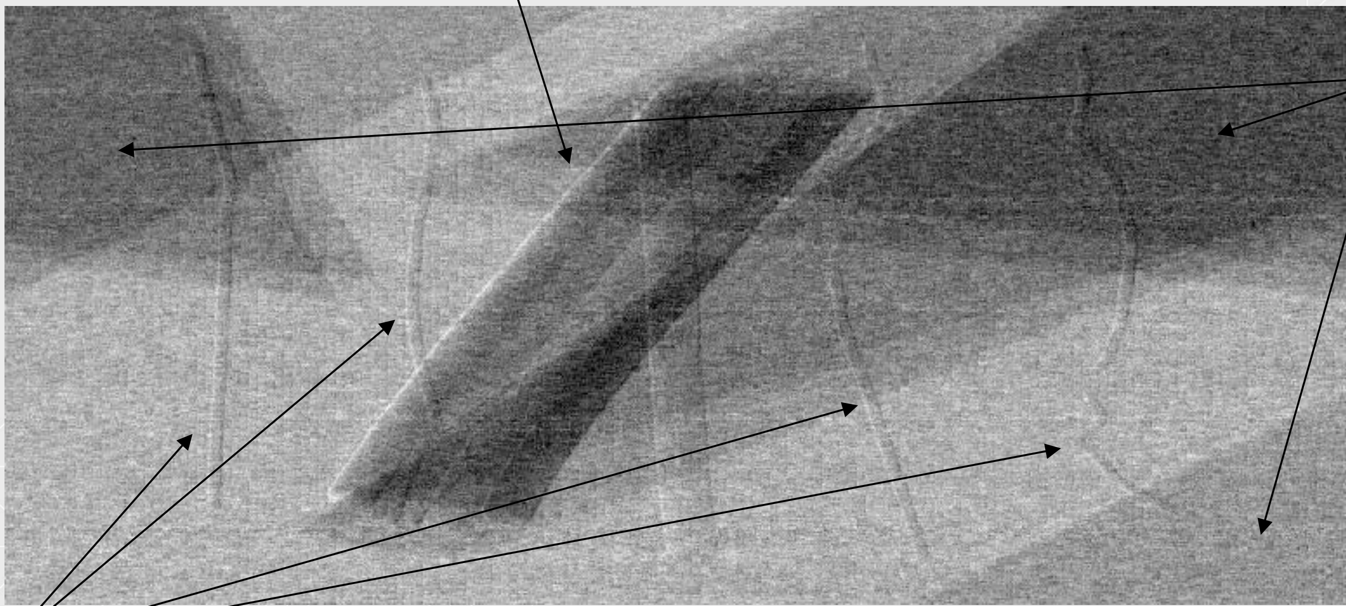
Endrizzi *et al*, JINST 8 (2013) C05008

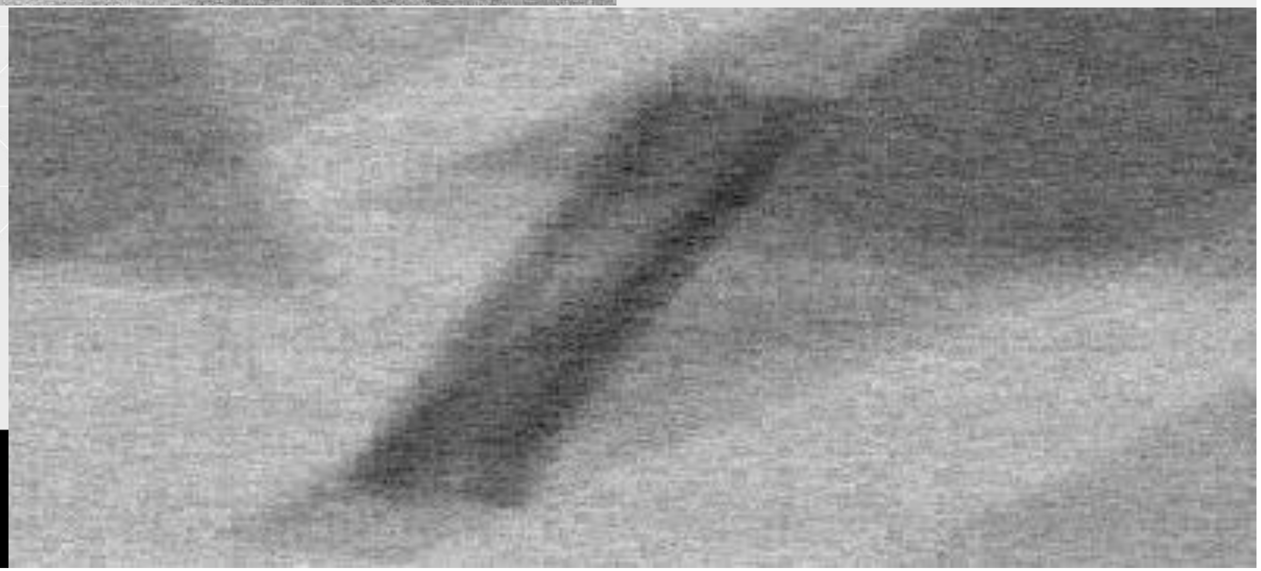
Non-medical applications 1: testing of composite materials



Endrizzi *et al*, proc. SPIE 8668 (2013) 866812

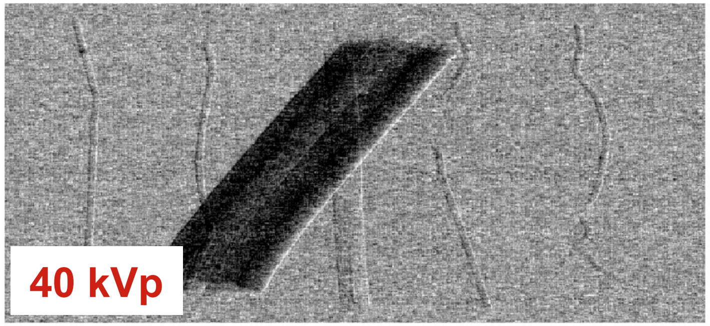
Non-medical applications 2: security scans

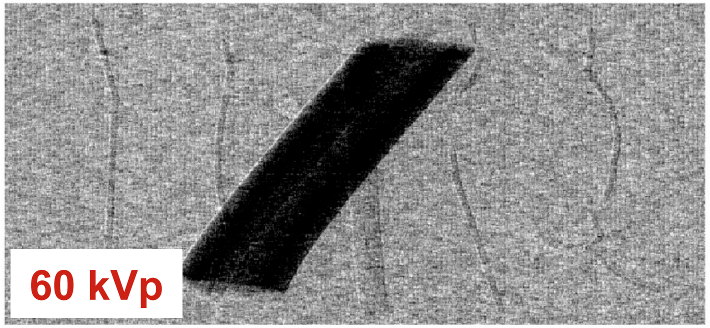


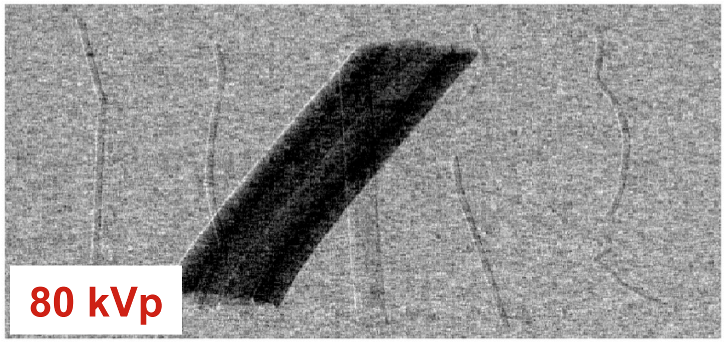


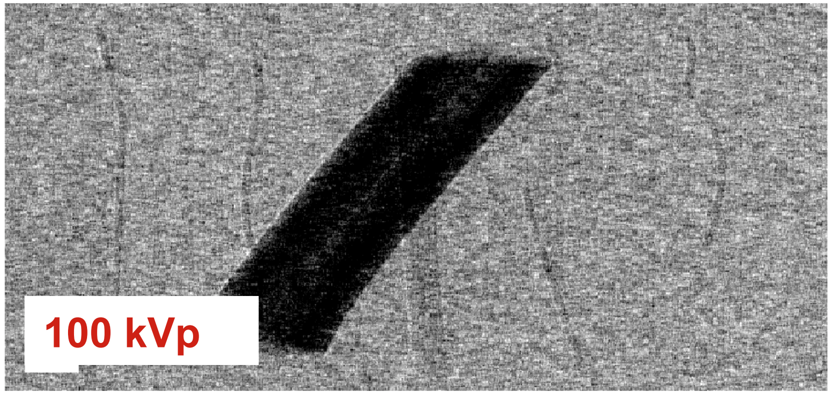
Olivo *et al* Appl. Opt. 50 (2011) 1765-9

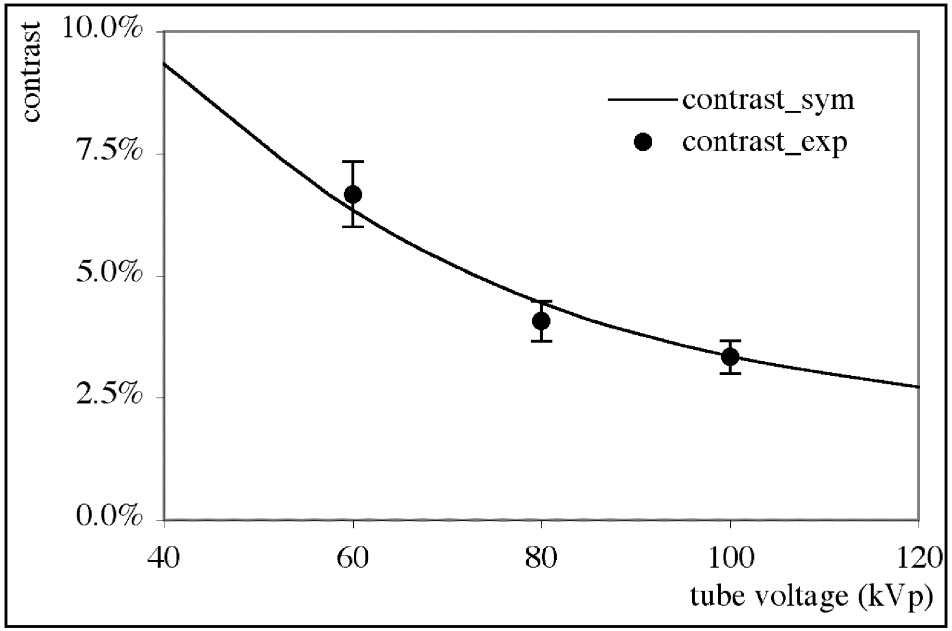
Phase contrast vs. x-ray energy







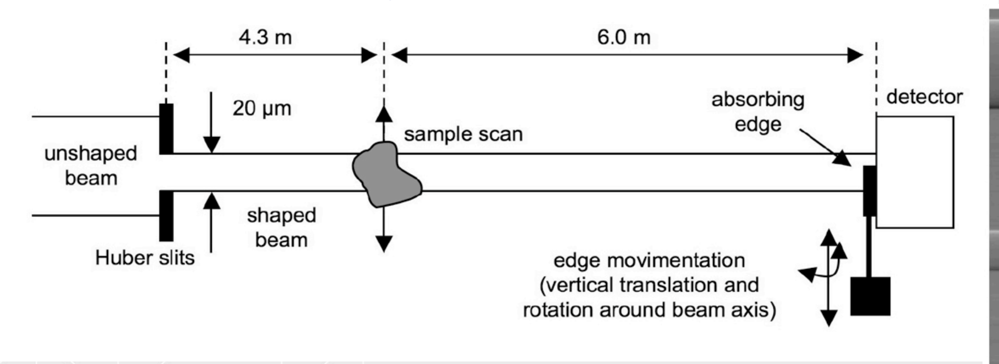


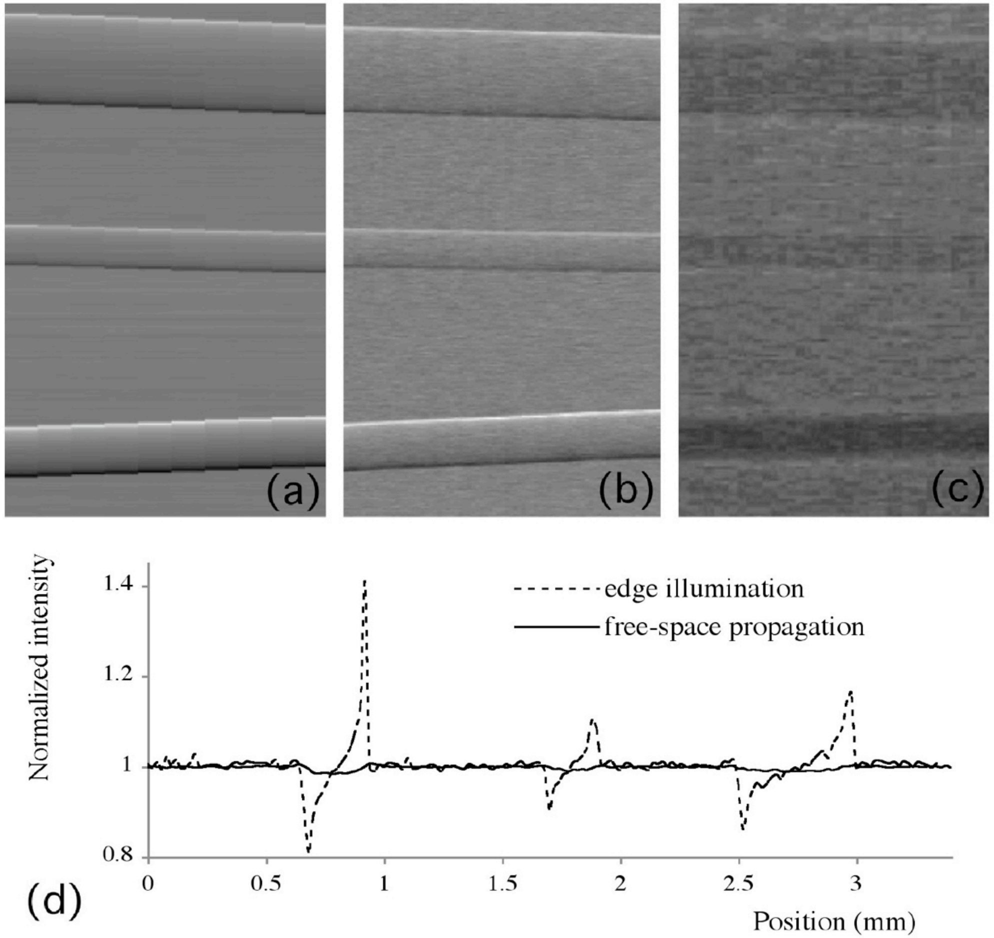


Ignatyev *et al*, J. Appl. Phys. 110 (2011) 014906

Even higher (monochromatic) energy - ESRF, 85 keV

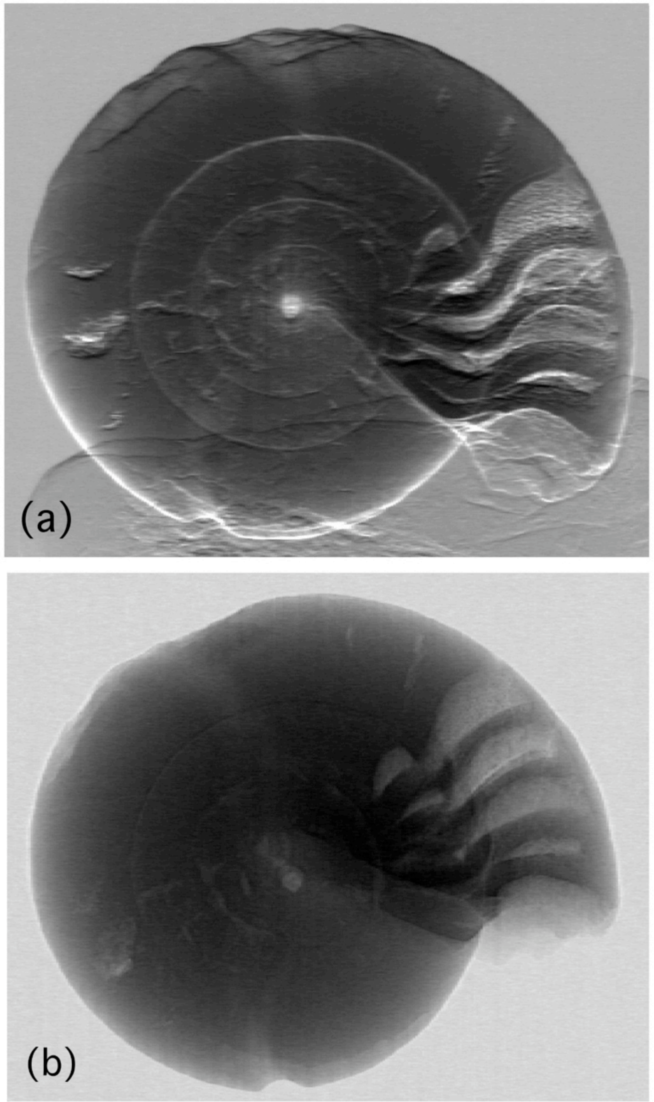
very simple set-up… **-> highly increased contrast!**





Olivo *et al*, Opt. Lett. 37 (2012) 915-7

Even higher (monochromatic) energy - ESRF, 85 keV



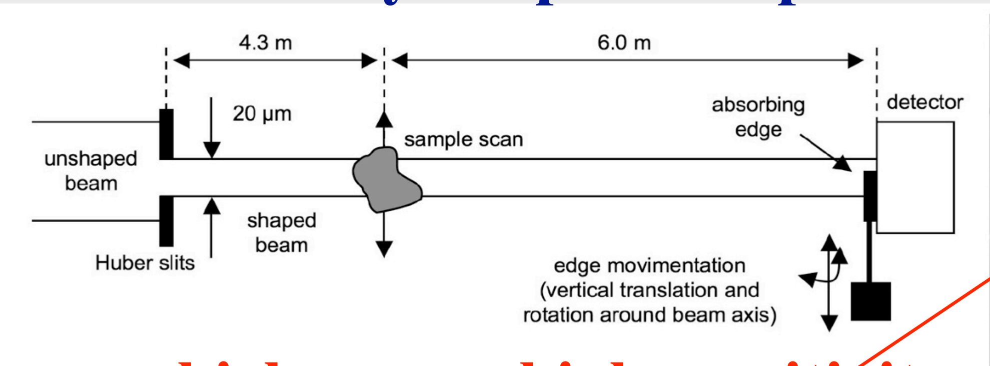
Edge illumination

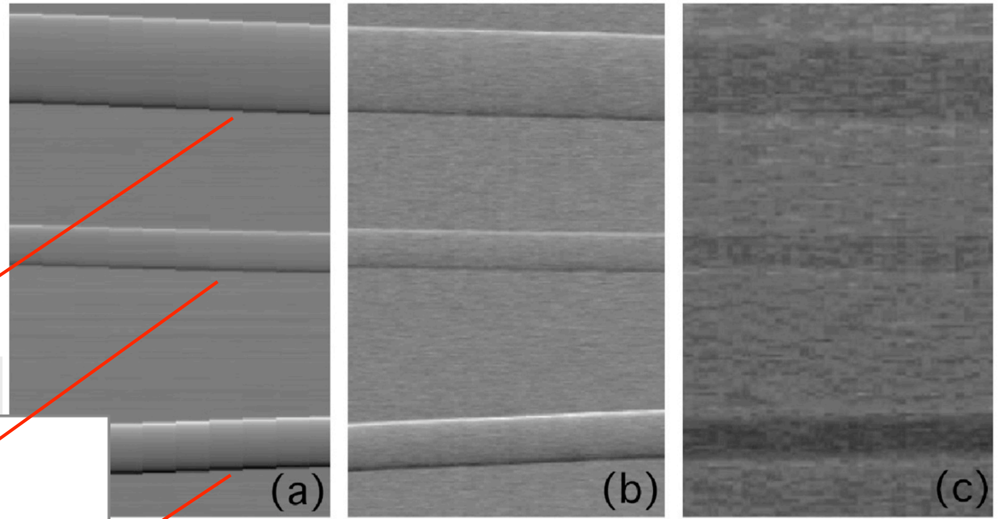
Free-space propagation

Olivo *et al*, Opt. Lett. 37 (2012) 915-7

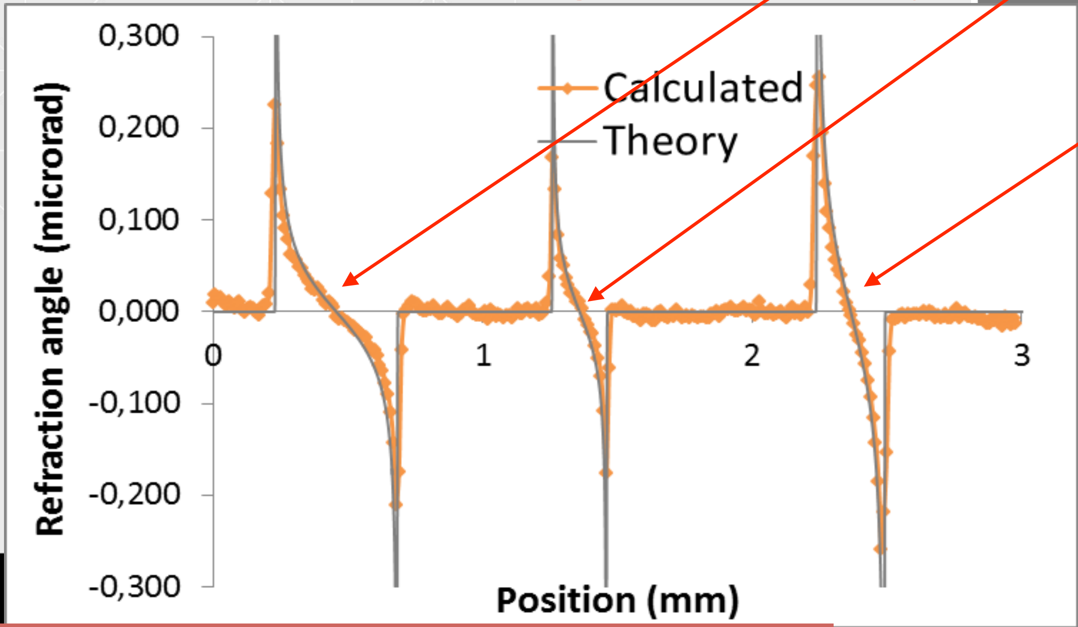
Even higher (monochromatic) energy - ESRF, 85 keV

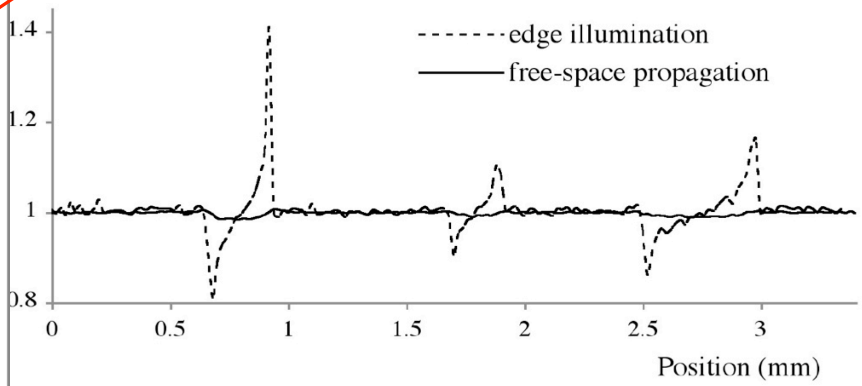
very simple set-up… -> highly increased contrast!





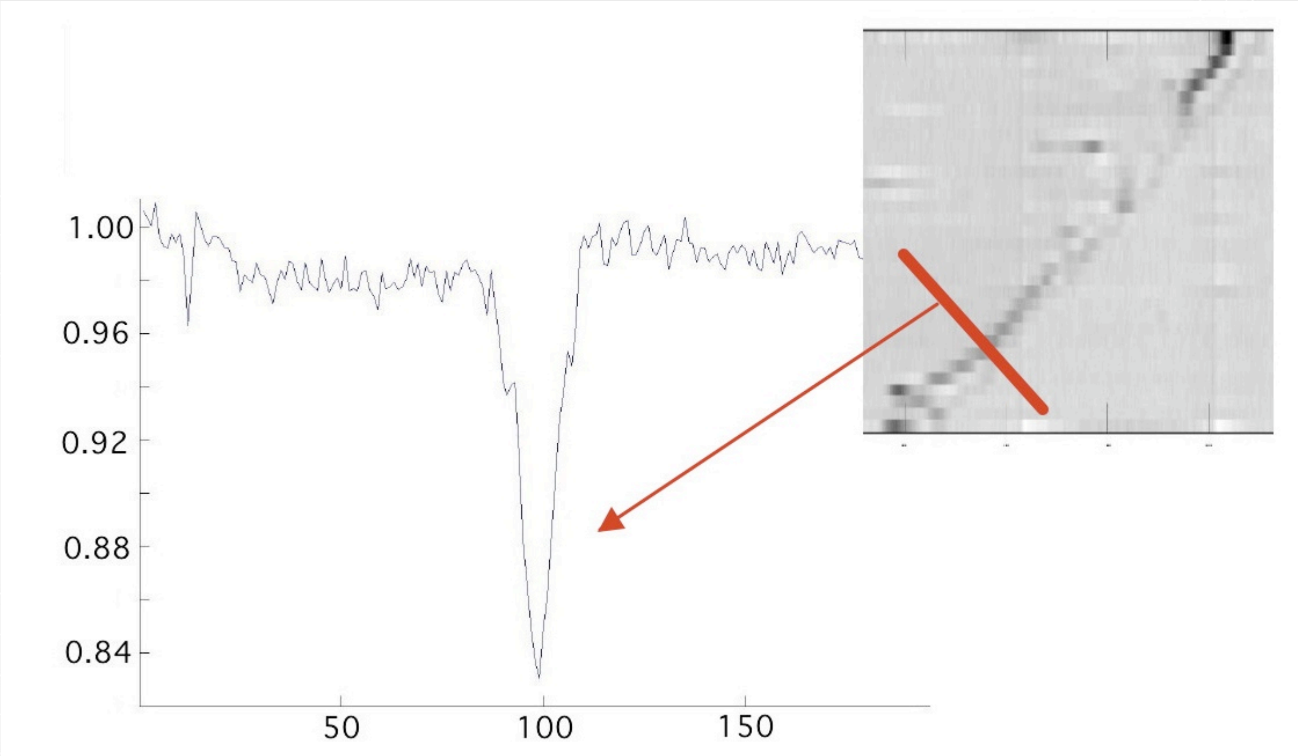
-> which means high sensitivity





Diemoz et al, Phys. Rev. Lett. 110 (2013) 138105

Exploitation of additional sensitivity to push the detection threshold further:



A 10 micron thick polyethilene foil immersed in water (-> matching refractive index!) generates an unprecedented **16%** image contrast!

Practically corresponds to a single cell in water

Diemoz et al, Phys. Rev. Lett. 110 (2013) 138105

Conclusions:

Coded-aperture XPCi is a NON-INTERFEROMETRIC, TOTALLY INCOHERENT, QUANTITATIVE x-ray phase contrast method working with conventional sources which:

allows the use of fully divergent, fully polychromatic x-ray sources with focal spots of up to at least 100 μm - with no additional collimation/aperturing; **the use of large apertures in thin gold layers** (-> no angular filtration), **low-absorbing graphite substrates, moderate misalignments between masks allowed achieving a reduction in the exposure times -** although demanding medical applications require further developments. Most of all they keep the **dose at acceptable levels**.

requires aperture pitches of the order of ~50-100 μm - therefore making fabrication, alignment and scale-up (masks are available up to 30 cm) easier.

has been described both by wave & geometrical optics (but for source sizes like the ones we use they give the same results) and **robust phase retrieval was achieved.**